Revista médica del
Hospital General de México

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CLINICAL CASE

Dengue-malaria coinfection by *Plasmodium falciparum* in a schoolchild

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Abstract

Introduction: *Dengue, yellow fever, malaria, and leishmaniasis are vector-borne infections.* **Objective:** *The objective of the study was to present a clinical case of severe malaria and dengue coinfection.* **Materials and methods:** *This was a descriptive study with the presentation of the clinical history and literature review.* **Results:** *A 10-year-old patient was admitted to the Hospital Militar Central in Bogotá, diagnosed with severe malaria by Plasmodium falciparum and dengue. He received intravenous fluids, acetaminophen, and three artemether-lumefantrine tablets every 12 h for 3 days. A literature review was done and the case findings were compared with what was published in databases.* **Conclusion:** *Malaria and dengue are frequent in tropical zones, but the probability of coinfection is low due to the variable presentation of these two diseases, and their prevalence depends on local endemicity.*

Key words: *Dengue. Malaria. Coinfection. Case.*

Introduction

Infectious diseases are caused by pathogenic microorganisms such as viruses, bacteria, parasites, or fungi. These diseases may be transmitted by vectors, including hematophagous insects, among people, or between animals and people in the case of zoonoses. Mosquitoes are the most widely known vectors that ingest the ineffective parasite forms present in the blood of a host (person or animal) and then later inoculate them in a new carrier, mainly through the skin or saliva.

Worldwide, more than 700,000 deaths are reported annually as a result of vector-borne diseases, including malaria, dengue, human African trypanosomiasis, leishmaniasis, Chagas disease, yellow fever, Japanese encephalitis, and onchocerciasis.

Dengue is an acute, viral, endemic, and epidemic disease transmitted by the bite of female mosquitoes of the *Aedes* genus, mainly *Aedes aegypti*. It currently constitutes the most important arbovirosis in the world in terms of morbidity, mortality, and economical impact since it is estimated that 3 billion people live in zones where there is a risk of contracting dengue. There are 390 million infections (96 million of them are asymptomatic) and 20,000 deaths due to this disease per year.

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Date of reception: 20-12-2018
Date of acceptance: 30-10-2019
DOI: 10.24875/HGMX.19000009

Available online: 17-01-2020
Rev Med Hosp Gen Mex. 2020;83(1):33-37
www.hospitalgeneral.mx

The etiological agent is the dengue virus (DENV), of the *Flavivirus* genus, and it has four serotypes (DENV1, DENV2, DENV3, and DENV4), which circulate simultaneously in Colombia. Its incubation period is between 4 and 10 days. The disease might be caused by any of the serotypes and it does not trigger cross-immunity. Thus, a person might contract the infection by the four serotypes and go through each course of the disease up to 4 times.

Malaria is caused by *Plasmodium* spp. parasites. It is an anthropozoonosis transmitted by infected female *Anopheles* spp. mosquito bites. There are five parasite species causing malaria in human beings. However, *Plasmodium falciparum* and *Plasmodium vivax* have the highest pathogenicity.

Infections caused by the DENV and the malaria parasite are serious enough given the fact that they appear as a cell or organism infection by two microorganisms simultaneously. Although dengue and malaria coinfection occurs, there is a lack of clinical suspicion and proper diagnosis in the concurrent infection. According to the World Health Organization (WHO), the coinfection caused by dengue and malaria in an individual is considered as a "severe malaria" case, and as such, it should be diagnosed early[1-3].

The objective of this report was to describe a *P. falciparum* and dengue coinfection case in a 10-year-old boy treated at the Hospital Militar Central in Bogotá and confronted with literature.

Case report

A 10-year-old male patient was referred from Quibdó (Chocó) with a 10-day evolution clinical picture of pulsing frontal headache, with mild-to-moderate intensity, previously associated with general discomfort, asthenia, adynamia, and abdominal pain in the epigastrium.

On the 9th day, the patient was found lying somnolent in bed and with signs of sialorrhea, closed eyes, and in fetal position. For this reason, he was taken to a first level health center where an episode characterized by hypersalivation, without abnormal movements or sphincter relaxation, and 3 min duration occurred. He was referred later to the second level hospital. During the ambulance ride, the patient presented with a new episode of similar characteristics and had a 38.3 - 39° C fever, so they started dipyrone treatment.

Hemoparasites and dengue clinical studies were conducted with negative results. The antibiotic treatment included penicillin G benzathine and ceftriaxone. Nevertheless, the fever persisted along with abdominal pain, headache, and vomiting. The patient was then referred to the Hospital Militar Central, with a diagnostic impression of an intracerebral expansive mass to be discarded, intracranial hypertension, and epilepsy.

Patient with a positive infection lesion, sisters with malaria diagnoses, and coming from an endemic region. Important medical background: fever seizure at 4 years of age followed by the second episode a year later. Surgical background: appendectomy and laparotomy (30 days earlier, which lead to a 3-day hospitalization). On arrival to the institution, the patient was received in a not so good state of health, hypotensive with a 65 mmHg average blood pressure, 126 bpm heart rate, feverish, dehydrated, oliguric, desaturated (84%) (FiO_2 21%), and bipalpebral edema. There was a 1 cm right posterior cervical adenopathy, painless and movable, and a painless 1 cm right anterior movable cervical adenopathy; abdomen showed evidence of a painful liver enlargement of 3 cm below the costal margin and palm and sole jaundice. Neurologically, the patient was alert, with bradilalia.

Paraclinical examinations

Hemogram

Leukocytes, 5225/mm^3; neutrophils, 44.5%; lymphocytes, 45%; monocytes, 8.8%; eosinophils, 1.10%; basophils, 0.6%; red blood cells, 4.32 M; hematocrit (HTO), 31.56%; hemoglobin (HB), 10.7 gr%; medium corpuscular volume (VMC), 72.9 fl; corpuscular media HB (HCM), 24.8 pg; wide distribution of erythrocytes (red cell distribution width), 14.1%; platelets 55,000/mm^3; prothrombin time (PT), 11.1 seg; control PT (PTC), 10.7 seg; partial thromboplastin time (PTT), 35.6 seg; PTT control, 29 seg; INR, 1; chlorine, 98 mEq/L; potassium, 3.4 mEq/L; sodium, 137 mEq/L; blood urea nitrogen (BUN), 7 mg/dl; creatinine, 0.5 mg/dl; uric acid, 2.1 mg/dl; lactate dehydrogenase, 319 UI/L; total bilirubin, 0.55 mg/dl; indirect bilirubin, 0.26 mg/dl; direct bilirubin, 0.29 mg/dl; aspartate transaminase, 39.64 UI/L; alanine transaminase, 66 UI/L; sodium, 137 mEq/L; potassium, 3.4 mEq/L; chlorine, 98 mEq/L; albumin, 2.93 g/d; creatinine, 0.5 mg/dl; BUN, 7 mg/dl.

Urine test

Slightly cloudy; pH 7.0; density 1020; negative esterase; negative nitrites; proteins, 25 mg; glucose, normal; ketones, 50 mg/dl; blood, negative; low epithelial cells; leukocytes, 2-4 × c, positive for bacteria, low mucus.

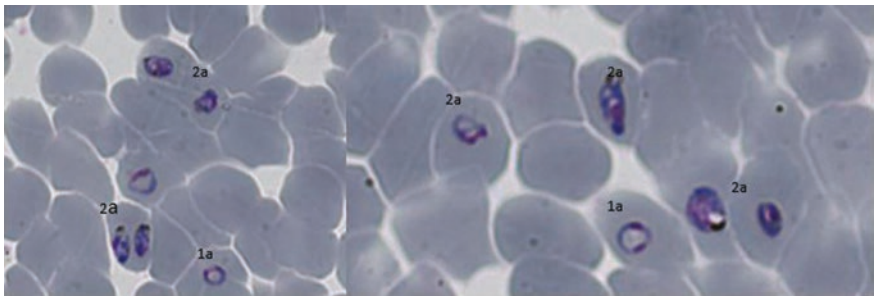

Figure 1. *Plasmodium falciparum*: parasitized erythrocytes are observed in a thick blood smear, Giemsa. 1a. Annular morphology trophozoites, double chromatin. 2a. Trophozoites in different development stages.

Negative Gram stain for microorganisms. Agsn1, negative, immunoglobulin G (IgG), and IgM positive for dengue.

Hemoparasites

Positive for *P. falciparum*. Asexual forms, 18,337/mm^3; IgM for cytomegalovirus, 1.28.

Peripheral blood swab

Moderate anisocytosis with microcytes. Some atypical lymphocytes can be observed in the white blood cells. Manual platelet count: 57,000/mm^3.

Abdominal ultrasound

Oversized liver and normal hyperrefringence of the intra- and extra-hepatic bile ducts. Permeable portal vein. Distended gallbladder, with enlarged walls (5 mm), without any pathological images inside. Sonographic Murphy sign: negative. Kidneys showed normal shape, size, and echogenicity. There were no pyelocalyceal dilatations or perirenal collections. The visualized areas of the pancreas (head and body) and the retroperitoneum showed no alterations. The spleen showed normal shape, size, and echogenicity without any injuries inside. Partially distended bladder, with thin walls, and no pathological images inside. Free fluid in the pelvis was observed. Intestinal loop distention with free fluid inside. Opinion: the previously described findings were probably related to a hepatic inflammatory process. The thorax ultrasound showed a bronchial inflammatory process and the simple skull scanography was normal.

The patient was diagnosed with a severe dengue infection with neurological compromise and with complex malaria considering the epidemiological, clinical, and laboratory criteria caused by *P. falciparum*. Using a thick smear test – which is the recommended test method by the WHO – we determined that the patient showed a parasitemia with 18,337/mm^3 asexual forms (Fig. 1); dengue was detected through serodiagnosis using the enzyme-linked immunosorbent assay test to detect IgM and IgG for dengue with 97% and 93% specificity, respectively. This is the most useful technique due to its sensitivity and accuracy when diagnosing infections caused by dengue.

Due to his clinical condition, treatment with intravenous liquids was established: acetaminophen and artemether-lumefantrine (3 tables every 12 h for 3 days) as it was malaria by *P. falciparum*.

Discussion

Malaria and dengue commonly occur in tropical zones. Nevertheless, the probability of coinfection is less common due to the varying presentation of these two diseases, taking into account that it depends on weather conditions such as altitude criteria for the reproduction of the vector. The mosquito vectors for dengue are the females of the genus *Aedes*, which have a diurnal hematophagous habit. The vector for *Plasmodium* spp. and *Anopheles* spp. has a strict nocturnal activity. In addition, their prevalences are in urban and rural areas, respectively, which lead to a concurrent infection by chance[4].

In a cross-sectional observational cohort study conducted between 2012 and 2015 in a dengue diagnosed patient at the Hospital Militar Central in Bogotá, the coinfection was cataloged as the third in frequency, being malaria most prevalent than any other etiologies. In the same study, low levels of simultaneous hematocrit with persistent fever were evidenced to show

coinfection whether bacterial, viral, or due to malaria[5]. The findings show similarities with those reported by Muhammad et al., in a study conducted in 2012 in Pakistan, where the presence of coinfection by dengue and malaria showed lower hematocrit levels, compared to the patients who presented with an infection exclusively for dengue (39.3% vs. 41.7%). Likewise, they stated that the coinfection was more severe than the unique infection with severe thrombocytopenia and anemia[6].

In our case, the main signs and symptoms to evaluate the coinfection were as follows: low levels of hematocrits, thrombocytopenia with no bleeding, painless hepatomegaly, slight elevation of transaminases, and palm and sole jaundice, as many of those symptoms, are within the most commonly reported in the textbooks. We also took into account that the patient's origin was an endemic zone and the fact that his two sisters also presented with symptoms and diagnoses of a malaria clinical picture.

In a transversal study conducted by Magalhães et al., in the Brazilian Amazonia region between 2009 and 2011, severe dengue symptoms such as vomiting, abdominal pain, and hepatomegaly occurred mostly in the coinfection cases, similar to this report, as they coincide and have the same symptomatology[7].

Arboleda et al. conducted a retrospective and descriptive study in the Hospital Antonio Roldán Betancur in Apartadó, Antioquia, Colombia, which showed that in 8 of the 45 reported dengue patients (17.7%), six had malaria by *P. vivax* coinfection, and two had malaria by *P. falciparum*. The patient's ages ranged between 6 months and 68 years with an age mean of 22.1 years[8]. This study has been, so far, the first coinfection publication which included the pediatric population; this case is the first report of a primary school patient. The possibility of a higher coinfection rate by dengue and malaria cannot be discarded given the prevalence of both infectious entities within the national territory.

In Colombia, approximately 12 million people inhabit zones at risk of malaria transmission, which makes it one of the most relevant contagious infections in the country. Its surveillance, prevention, and control are highly important for public health measures. In this country, malaria zones are between 0 and 1600 m above sea level, i.e., the coastal regions, Cauca river low valleys, and high Sinú, the Amazon, and Orinoquia are at a higher risk.

As such, 92.2% of the country's territory is considered as a potential endemic area since it has the specific ecological and epidemiological conditions for the infection. Even if the mortality rates have decreased within the country, the morbidity remains high at about 150,000 cases/year and a mortality rate between 65 and 165 deaths/year in the past decade. According to the last report from the Sistema de Vigilancia de Salud Pública of the Instituto Nacional de Salud (SIVIGILA-INS), in the past 2 years, between 20 and 60 deaths were reported, respectively.

The infection prevalence by species in Colombia, according to their distribution, is established as follows: *P. vivax,* 63.3%; *P. falciparum*, 36.3%; *P. malariae*, 0.025%, and 2% of the total cases corresponded to a mixed infection caused by *P. falciparum* and *P. vivax*. *Plasmodium ovale* has only been reported in one episode in the country in the past decade, and it took place in the Caribbean region.

During the 26th epidemiological week, SIVIGILA had registered 29,603 cases of malaria; 29,130 of these cases were caused by malaria without complications and 473 with complications. It also showed an increase in the reporting of cases for the biogeographical territorial region of Northern Santander when compared to the average recorded in the period between 2012 and 2017. By origin, Chocó, Nariño, Córdoba, Antioquia, Guainía, Amazonas, Bolívar, and Cauca departments reported 88.7% of the cases of malaria with no complications. Chocó accounted for 27.3% of the reports[9].

For the case of infection by dengue, based on the SIVIGILA report, up to the 44th week in 2017, there were 23,188 cases for the national territory, from which 13,647 (58.9%) gave no alarm signs, 9,270 (40.0%) showed signs, and 271 (1.1%) were reported as severe dengue; 80.4% originated in the following departments: Valle del Cauca, 18.9%; Antioquia, 17.4%; Tolima, 11.0%; Santander, 7.8%; Huila, 5.0%; Meta, 4.9%; Norte de Santander, 4.2%; Cundinamarca, 4.1%; Cesar, 2.7%; Córdoba, 2.3%; and Quindío, 2.2%. Among relevant aspects, it is noteworthy that 57.1% of the infections occurred in males, 14.4% of the reported cases for severe dengue were in children younger than 5 years of age, and the frequency by ethnic group was 763 (3.3%) in African Colombian population, and 269 (1.2%) in indigenous population[10].

Conclusion

Dengue and malaria are part of the infections transmitted by common tropical zone vectors. However, the coinfection diagnosis is a medical challenge given the variability of its presentation, making it crucial to remember that the coinfection prevalence depends on the local endemicity.

More research about the coinfection frequency for dengue and malaria is needed as Colombia is an endemic and epidemic region for both.

Acknowledgments

The authors would like to thank the Hospital Militar Central, the Facultad de Medicina of the Universidad Militar Nueva Granada, and to Orlando Torres-Fernández and Gerardo Santamaría-Romero from the Grupo de Morfología Celular of the Instituto Nacional de Salud.

Conflicts of interest

The authors declare that they have no conflicts of interest.

Funding

The authors did not receive any funding to develop this research. The patient was hospitalized in the Hospital Militar Central.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors have obtained the written informed consent of the patients or subjects mentioned in the article. The corresponding author is in possession of this document.

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