CASE REPORT

A case of severe dengue in a 5-year-old boy in the city of Lima

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ABSTRACT

Dengue is a viral infection which is transmitted by the *Aedes aegypti* mosquito and has four serotypes (DENV-1 to DENV-4). The disease triggers a variety of clinical manifestations, ranging from mild forms without warning signs to severe life-threatening forms. We present the case of a 5-year-old boy, from the province of Callao, whose first symptoms were fever, headache and general malaise. On the third day, the child had mild abdominal pain and little vomiting; subsequently, abdominal distension, jaundice and choluria. He was admitted to the pediatric intensive care unit being alert and with moderate dehydration, jaundice, edema, distended and tender abdomen, shifting dullness and liver 2 cm below the right costal margin. Complementary tests revealed liver failure, hepatosplenomegaly and pleural effusion in the bases. Using a reactive IgM ELISA, severe dengue was diagnosed, as well as a superinfection due to probable spontaneous bacterial peritonitis. He started treatment with antibiotics, furosemide, fresh frozen plasma, cryoprecipitate and metamizole. As the child did not get better, the diuretic was optimized, and human albumin was administered. Thereafter, he got better showing decreased ascites, edema, jaundice and pleural effusion; improvement of the liver and coagulation profile; and being afebrile. He unexpectedly presented respiratory distress due to congestive heart failure caused by dilated cardiomyopathy diagnosed by echocardiography; thus, he was treated with diuretics. The patient was discharged afebrile, without edema and with resolution of liver failure and coagulation disorder.

Keywords: Dengue; Aedes; Severe Dengue; Child (Source: MeSH NLM).

INTRODUCTION

Dengue is a viral infection transmitted through the bite of *Aedes aegypti* mosquito. The pathogen is called dengue virus (DENV) and has four serotypes: DENV-1, DENV-2, DENV-3 and DENV-4 [1]. This RNA virus belong to the species dengue virus, genus *Flavivirus*, family *Flaviviridae* [2]. The vector, *Aedes aegypti*, is a daytime peri-domiciliary mosquito that is capable of reproducing in various containers that can store water [3].

Following the bite of an infected mosquito, the virus replicates in the host, particularly in dendritic cells and regional lymph nodes [2], and after infecting macrophages, monocytes and lymphocytes, it is disseminated to other tissues through the lymphatic system and blood [4]. DENV infection triggers a variety of clinical manifestations, from a mild flu-like syndrome, known as dengue fever, to the potentially fatal dengue shock syndrome [1].

Infection with a strain is followed by up to three outcomes: a) long-lasting protection against infection with the same strain, b) brief protection against infection or disease with a different strain, and c) an infection with a different strain that may result in severe disease [5]. There are noteworthy predictors for the development of severe dengue: being a child, secondary infection, diabetes and renal diseases [6]. Research studies have been conducted in Peru involving a traceability to household members. The concept that the risk of DENV infection is related to the presence or absence of the vector in the places visited during the day has been reinforced. In addition, it was evidenced that sick individuals do not significantly spread DENV [5]. Epidemiologically speaking, it is important to highlight that drastic environmental changes related to global warming have become evident in recent decades, and this fact facilitates a wider geographic distribution of the vector. Other factors are related with the conservation of objects that serve as mosquito breeding sites [3].

It is important to emphasize that a serotype of dengue producing lifelong immunity against reinfection, but it provides only temporary and partial immunity against other serotypes [2]. Infants with primary dengue infections whose mothers have some immunity against the disease and children who become infected with a second dengue

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serotype after an initial primary infection are at increased risk of progressing to the severe form [4].

There is in vivo evidence that tissue-damaging DENV non-structural protein 1 (NS1) is responsible for most of the pathophysiological characteristics of severe dengue. This protein is used as a marker for diagnosing the pathogen [5].

The laboratory diagnosis can be determined within five days from the onset of the disease through the direct detection of viral components in serum (NS1 antigen detection), polymerase chain reaction and viral culture. After day 5, the serological diagnosis provides indirect evidence of dengue through IgM and IgG markers [4].

CLINICAL REPORT

We present the case of a five-year-old male patient, native to the province of Callao, whose house was located in the district of Ventanilla, with no significant pathological history. He visited the Emergency Service of Hospital Nacional Daniel Alcides Carrión (HNDAC), taken by his mother. He had been sick for 10 days, with insidious onset and progressive course. His first symptoms were a fever of 39°C, headache, conjunctival discharge and general malaise, for which his mother administered paracetamol. Three days later, he had mild abdominal pain and hyporexia. Therefore, he was taken to a healthcare center, where he was given metamizole and the same drug was prescribed for home use every eight hours. After two days, he had post-prandial vomiting (three times a day); the next day he had abdominal distension, yellowing of his sclerae and choluria. Subsequently, he was taken to the Emergency Service because the abdominal pain increased and the fever persisted, in addition to presenting other symptoms. Consequently, he was hospitalized in the Pediatric Intensive Care Unit (PICU) of HNDAC. The physical examination revealed that his heart rate (HR) was 110 beats per minute respiratory rate (RR) 28 breaths per minute (bpm), blood pressure (BP) 112/57 mmHg, pulse 55, mean arterial pressure (MAP) 75, T 39 °C and O_2 saturation 98 %, as well as sunken eyes, semidry oral mucosa, icteric sclerae, bilateral palpebral edema, warm and icteric skin, without palpable lymphadenopathy. In the respiratory system, diminished vesicular breath sounds was appreciated at the bases of both hemithoraxes. Heart sounds were rhythmic and of good intensity. The abdomen appeared globular, distended, with pain upon superficial and deep palpation, shifting dullness, liver palpable 2 cm below the right costal margin, with an abdominal perimeter of 62 cm. Edema was observed in the feet. The patient was awake and lucid, oriented to time, space and person.

The laboratory tests at the hospitalization evidenced liver failure with moderate hypertransaminemia (glutamate oxaloacetate transaminase [GOT] of 661 U/L, glutamate pyruvate transaminase [GPT] 187 U/L, total bilirubin [TB] 5.20 mg/dL, direct bilirubin [DB] 2.056 mg/dL, Alb 1.75 g/dL), severely altered coagulation profile (thrombin time [TT] 33.8", prothrombin time [PT] 22" 48 %, activated partial thromboplastin time [APTT] 52.7", fibrinogen 78 mg/dL, international normalized ratio [INR] 1.68 and D-dimer 10.34 ug/dL). The blood cell count showed the following results: leukocytes 13,000, neutrophils 6,210, lymphocytes 5.8, hemoglobin 8.4 g/dL, hematocrit 25.7 % and platelets 422,000, C-reactive protein (CRP) 20 U/L, lactate dehydrogenase (LDH) 2,100 U/L and ferritin 2,000 mg/L. The abdominal ultrasound revealed hepatosplenomegaly, and the chest X-ray showed pleural effusion in the bases of both hemithoraxes.

At the time of hospitalization in the PICU, the following diagnoses were considered: febrile jaundice syndrome, with the differential diagnosis including leptospirosis and viral hepatitis. Therefore, he was evaluated by the infectious disease specialist, who suggested the possibility of severe dengue fever, which was confirmed by a reactive ELISA Ig M result. The severity criteria comprised ascites, pleural effusion, hepatitis and disseminated intravascular coagulation. Due to the presence of a high fever, significantly increased CRP, leukocytosis and abdominal involvement; thus, bacterial superinfection—e.g., spontaneous bacterial peritonitis—was suspected. Treatment was initiated with 5 % dextrose, fresh frozen plasma, cryoprecipitate, posttransfusion furosemide, piperacillin/tazobactam plus metronidazole and administration of metamizole conditional upon fever. Continuous monitoring of vital functions, hemodynamics, diuresis, bleeding with strict water-electrolyte balance was established.

Despite treatment, the severity of the patient's condition remained stationary: liver and coagulation profiles were unchanged while albumin remained low; additionally, there was an increase in ascites (abdominal perimeter of 68 cm), positive water balance, diuresis exceeding 1 mL/kg/h, scrotal edema and respiratory distress. In his condition, on the ninth day of hospitalization, Gastroenterology did not authorize therapeutic paracentesis due to the risk of bleeding. Instead, it was decided to optimize the management of diuretics (spironolactone plus furosemide according to posology), to start with the administration of daily human albumin and discontinuation of fresh frozen plasma and cryoprecipitate (Figure 1).

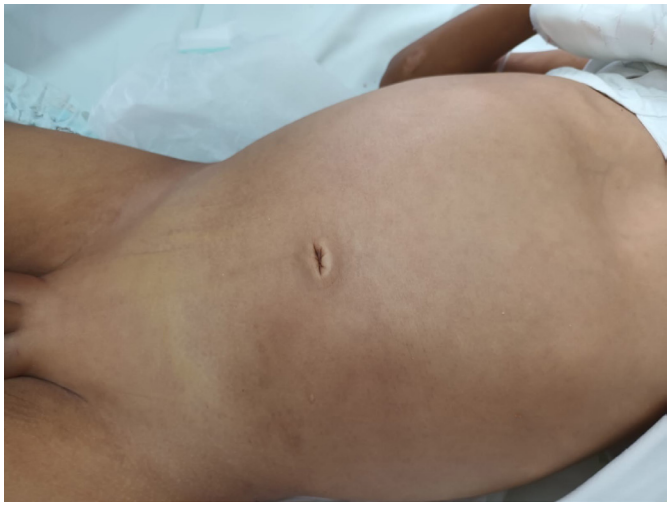

Figure 1. Distended abdomen due to severe ascites

The patient began to have increased diuresis with progressive negative water-electrolyte balances. With the new treatment, the abdominal perimeter was reduced to 64 cm; in addition, there was a decrease in scrotal edema and disappearance of edema in his lower limbs. Likewise, there was an improvement in the liver profile (GOT 265, GPT 66 and albumin 3.61) and the coagulation profile (PT 14.5" 87 %, APTT 33.9", INR 1.09 and fibrinogen 177). On the twentieth day of hospitalization, the patient was afebrile, the scrotal edema had disappeared, and his abdominal perimeter was 58 cm. He had no jaundice on his skin and only mild jaundice in his sclerae; furthermore, there was there was improvement in the liver profile (TB 2.39, DB 1.82, GOT 81 and GPT 35) and the coagulation profile (PT 13.9, APTT 32.9, INR 1.04 and fibrinogen 274). In addition, the following results were obtained: LDH 1,087, ferritin 2,000 and CRP 1.53. He received antibiotic therapy for 14 days, albumin for nine days, and furosemide as a continuous dose for three days, followed by bolus dosage after the administration of albumin. The next day, he presented with respiratory difficulty; thus, a chest X-ray was taken, revealing cardiomegaly and pulmonary congestion. The cardiologist diagnosed congestive heart failure due to dilated cardiomyopathy.

The echocardiogram evidenced left ventricular systolic dysfunction, with a left ventricular ejection fraction (LVEF) of 39 %, D-dimer 6.98 ug/mL, ferritin 522 ng/mL, TB 1.72, GOT 49, GPT 30, creatinine (Cr) 0.47 and CPK MB 12.20. Therefore, the prescribed treatment was captopril 6.25 mg po every 12 hours and carvedilol 3.125 mg po every 12 hours, and he continued his treatment with diuretics. Finally, he was discharged afebrile, without edema and with resolution of liver failure and coagulation disorder (Figures 2 and 3).

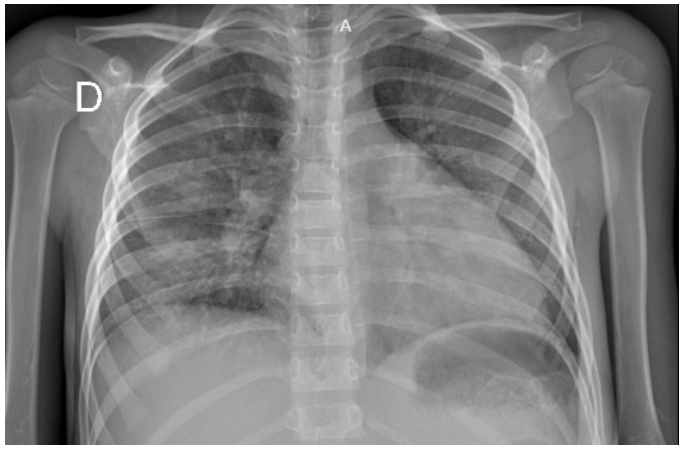

Figure 2. Chest X-ray showing severe cardiomegaly and pulmonary congestion

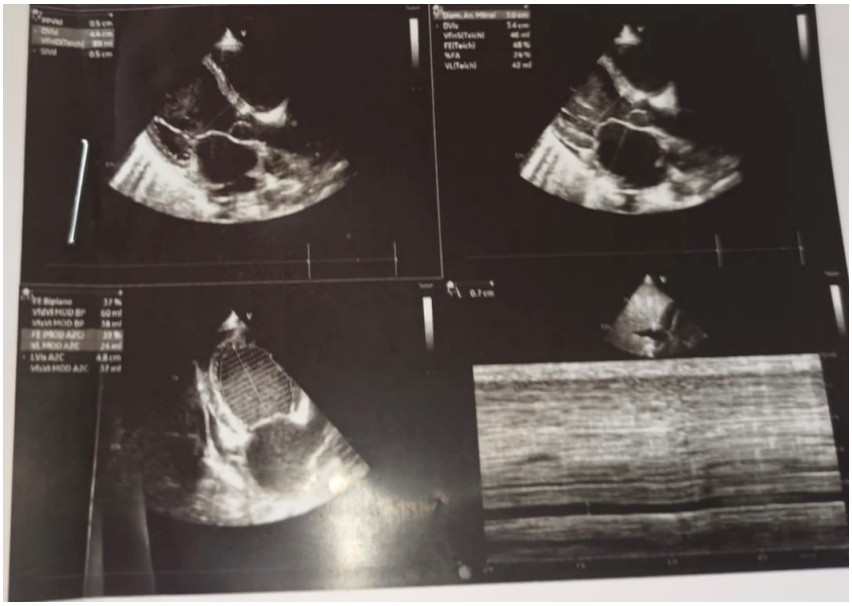

Figure 3. Echocardiogram showing a spherical image of ventricular cavities with global hypokinesia, leading to left ventricle systolic dysfunction. Flows of mitral and pulmonary regurgitation can be observed.

DISCUSSION

Dengue is a viral disease that more than a few authors have categorized as a "neglected tropical disease" [2]. Although mortality from severe dengue may not reach the high levels seen in diseases that are equally or more significant in public health [3], it is forecasted that climate change will further increase the population at risk of contracting dengue due to increased transmission in endemic areas and the expansion of the geographic range of *Aedes* mosquitoes [7].

In 2023, Peru experienced an epidemic that led to the declaration of a sanitary emergency in 13 departments in February. At the national level, up to the fourteenth epidemiological week, 40,958 cases were reported, with 42 deaths. Ucayali, Madre de Dios, Loreto, Piura, San Martín, Tumbes, Amazonas, Huánuco and Ica were the departments with the highest indicators. In the fourteenth week, a first outbreak was reported in the district of San Juan de Lurigancho in Lima [8].

After an asymptomatic incubation period of 4-10 days, the disease begins abruptly and is followed by three phases: febrile, critical and recovery. The day of defervescence, when the fever disappears, or day zero, is the crucial day for the patient: they either progress towards healing or towards forms that involve warning signs and severity [9]. The identification of this moment is crucial for timely case management.

The severity of the disease depends on the viral load and the magnitude of acute phase reactive substances (cytokines) [9]. Children are at higher risk of developing severe plasma leakage and progressing to dengue shock [10], as in the case of the patient who presented severe ascites, moderate pleural effusion, edema of the lower limbs as well as scrotal and bilateral palpebral edema.

From the pathophysiological standpoint, the severe form is characterized by increased vascular permeability, hypovolemia and abnormalities in hemostasis. The virus has a multisystemic impact due to its marked tropism for the organs of the monocyte-macrophage system, such as the bone marrow, spleen, liver and lymph nodes [11]. A review of cases reported occurrences of hepatitis, encephalitis, glomerulonephritis, hemolytic uremic syndrome, myocarditis, pulmonary hemorrhage and pancreatitis [9]. It is appropriate to include even encephalomyelitis, though it is a rare neurological complication. Cases have been reported such as that of a 6-year-old boy who developed neurological symptoms on the seventh day of the disease. Magnetic resonance imaging (MRI) showed acute disseminated encephalomyelitis, for which intravenous methylprednisolone was administered. He was discharged two weeks later, indicating that, although it is a serious complication, early recognition and timely treatment of encephalomyelitis can lead to a successful outcome without neurological sequelae [12].

The patient developed severe hepatic failure associated

with disseminated intravascular coagulation, cardiac failure due to dilated cardiomyopathy and renal damage with proteinuria. Moreover, proteinuria has been observed in other cases, such as an eight-year-old boy admitted to intensive care for severe dengue, who developed proteinuria shortly after reaching his lowest level of thrombocytopenia. The author highlights that dengue can cause a wide spectrum of acute kidney injury; however, proteinuria is a rare complication in this condition [13].

The study of hepatic alterations in patients with dengue is particularly relevant since signs and symptoms or altered liver profile often occur and are usually misinterpreted as having a different etiology than dengue. Moreover, there is adequate and timely management of these alterations [11]. Although liver involvement is not frequent in dengue, this damage is not attributable to this disease, but to other influential external factors, such as drug toxicity (e.g., caused by metamizole or other NSAIDs) [14].

Marianneau highlights that hepatic alterations are signs of poor prognosis and characteristics of a probable fatal disease [15]. Liver involvement is an unusual manifestation of dengue, although some authors state that it occurs with some frequency. Additionally, it has been described that the virus can cause moderate to severe liver dysfunction, with marked elevation of transaminases similar to that seen in viral hepatitis [16]. From the anatomopathological standpoint, focal hepatocyte necrosis, the presence of Councilman bodies and swelling with hyaline necrosis are described [11]. In severe forms, liver involvement is characterized by a significant elevation of transaminases that normalize by the second or third week, although it may persist for up to eight weeks [11,14].

Another criterion of severity is massive hemorrhage due to coagulation disorders and infection-induced thrombocytopenia. Some studies do not find any association between bleeding and thrombocytopenia [17], while others find a significant association when thrombocytopenia is less than 50,000/mL [18]. Thrombocytopenia in dengue may result from decreased production and increased peripheral destruction due to splenic sequestration and lysis by antiplatelet antibodies. Sabatier described that hemoconcentration and thrombocytopenia are not always present, even in patients with severe forms, with or without shock [19].

Coagulation disorders due to dengue have been associated with bleeding resulting from alterations of anticoagulant proteins. A Colombian research group found that significant bleedings were associated with a notable increase in PT and PTT [20]. Coagulation disorders, in combination with severe thrombocytopenia and other side effects of shock conditions—such as hypoxia, acidosis and decrease in fibrinogen—may lead to true disseminated intravascular coagulation. This patient had severe coagulation disorders; however, no bleeding of any kind occurred, probably because there was no platelet disorder. Clearly, there are cases where bleeding does occur and even blood transfusion is necessary, as reported in a case series of 10 severely ill dengue patients, where the need for blood transfusion was quickly recognized during the clinical course and for the benefit of the patients [21].

Capillary leak is accompanied by pleural effusion, ascites, edemas, organ impairment and shock. There is a greater propensity in children due to the fact that, intrinsically, their microvasculature is more permeable and has less capacity to compensate for plasma extravasation. Hypoalbuminemia is also considered to be a risk factor for the development of severe forms of dengue [19]. This hypoalbuminemia, as well as proteinuria, is frequent in dengue infection; therefore, it is important to consider it, particularly because the characteristics of dengue infection may mimic nephrotic syndrome in clinical practice [22].

Generally, when the fever goes down, if vascular permeability increases, it may progress to hypovolemia and, in some cases, lead to shock. During the initial stage of shock, systolic blood pressure remains normal, but with reduced cutaneous perfusion, resulting in cold extremities and delayed capillary refill time. If hypovolemia persists, systolic pressure drops while diastolic pressure is maintained. The result is a decrease in pulse pressure and mean arterial pressure [10]. These two pressures should be monitored because patients with alarm signs may progress to severe forms with shock. However, probably due to timely and adequate management, our patient did not develop an evident shock condition.

Some patients with dengue have a fever for more than ten days; in such cases, coinfection or superinfection must be ruled out. If there is leukocytosis with increased neutrophils and a significant elevation of CRP, the presence of an additional bacterial infection should be investigated. On admission, our patient presented leukocytosis, a markedly elevated CRP and persistent fever for more than 14 days. Therefore, a bacterial peritonitis superinfection was suspected, and antibiotic treatment was started. After 14 days of therapy, the fever disappeared, CRP normalized, and leukocyte levels returned to normal ranges.

It has been suggested that some early measures—such as appropriate fluid support and early hospitalization—along with the proper use of antipyretics could decrease the severity of the disease [20]. This calls for early recognition of certain prognostic indicators of higher risk of developing severe forms. Likewise, hypotension is a late sign of shock, and clinical surveillance of patients with dengue should aim to identify early clinical signs and symptoms indicative of tissue perfusion disorders (the initial phase of shock), such

as distal coldness and delayed capillary refill [23], in addition to recognizing warning signs that indicate the possible time of transition to severe forms of the disease [10].

Furthermore, it should be noted that other systems or organs may be affected, although in this specific case this did not occur. Castellanos et al. described cases of children diagnosed with dengue who presented neurological disease with characteristic signs such as tonic-clonic convulsions, alterations of consciousness, irritability and ataxia. Such authors highlighted the importance of including dengue as a differential diagnosis in neurological patients from endemic areas [24]. Similarly, rare cases of hemophagocytic syndrome have been described, such as that of a two-year-old boy with severe dengue who developed such syndrome but recovered after corticosteroid therapy [25]. In this regard, hemophagocytic lymphohistiocytosis—a rare fatal disease affecting lymphocytes and histiocytes—has been described [26,27], e.g., the case of a patient with dengue who progressed to this condition during his hospitalization. As the patient was clinically stable and there was a clear triggering condition such as dengue, supportive measures were chosen instead of condition-specific therapy. Despite our patient did not have these complications, it is important to know that early recognition is associated with better outcomes [27].

We believe that adequate knowledge of the disease can help in the timely diagnosis and appropriate management of cases, thereby preventing, whenever possible, the increased morbidity and mortality resulting, sometimes, from misdiagnosis and inadequate treatment since there have been reports of complications due to overhydration as well as the use of contraindicated medication, such as anticoagulants, corticosteroids and NSAIDs. Clear indications exist for the timing of packed red blood cell, fresh frozen plasma, cryoprecipitate and platelet in patients with severe dengue. Additionally, there are well-developed national and international guidelines and protocols, which should be implemented at diverse levels of healthcare in rural and urban populations. This work is expected to enable physicians to make appropriate and timely decisions in clinical practice and to establish adequate therapeutic measures aimed at reducing the morbidity and mortality of dengue.

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BIBLIOGRAPHIC REFERENCES

1. Harapan H, Michie A, Sasmono RT, Imrie A. Dengue: A minireview. Viruses [Internet]. 2020;12(8):829
2. Roy SK, Bhattacharjee S. Dengue virus: epidemiology, biology, and disease aetiology. Can J Microbiol [Internet]. 2021;67(10):687–702
3. Wilder-Smith A, Ooi EE, Horstick O, Wills B. Dengue. Lancet [Internet]. 2019;393(10169):350–63.
4. Verhagen LM, de Groot R. Dengue in children. J Infect [Internet]. 2014;69(1):77-86.
5. Halstead S. Recent advances in understanding dengue. F1000Res [Internet]. 2019;8:1279.
6. Tsheten T, Clements ACA, Gray DJ, Adhikary RK, Furuya-Kanamori L, Wangdi K. Clinical predictors of severe dengue: a systematic review and meta-analysis. Infect Dis Poverty [Internet]. 2021;10(1):123.
7. Wong JM, Adams LE, Durbin AP, Muñoz-Jordán JL, Poehling KA, Sánchez-González LM, et al. Dengue: A growing problem with new interventions. Pediatrics [Internet]. 2022;149(6):e2021055522.
8. Ministerio de Salud. Boletín Epidemiológio del Perú. Volumen 32 - SE14 (Semana epidemiológica del 2 al 8 de abril del 2023) [Internet]. Centro Nacional de Epidemiología, Prevención y Control de Enfermedades - Ministerio de Salud; 2023. Available from: https://www.dge.gob.pe/epipublic/uploads/boletin/boletin_202314_05_110922.pdf
9. Pizarro D. Dengue, Dengue hemorrágico. Acta pediátr costarric [Internet]. 2009;21(1):8-17.
10. Ministerio de Salud Pública y Bienestar Social - Asunción-Paraguay. Dengue: Guía de Manejo Clínico [Internet]. Ministerio de Salud Pública y Bienestar Social; 2012. Available from: https://iris.paho.org/bitstream/handle/10665.2/10101/9789996768422_esp.pdf?sequence=1&isAllowed=y
11. Larreal Y, Valero N, Estévez J, Reyes I, Maldonado M, Espina LM, et al. Alteraciones hepáticas en pacientes con dengue. Invest clín [Internet]. 2005;46(2):169-78.
12. Kamath N, Mounica K, Kanthila J, Kamath SP, Rao SS. A case report of acute disseminated encephalomyelitis following severe dengue in a child. Germs [Internet]. 2020;10(2):115–9.
13. Hebbal P, Darwich Y, Fong J, Hagmann SHF, Purswani MU. Nephrotic-range proteinuria in an eight-year-old traveler with severe dengue: Case report and review of the literature. Travel Med Infect Dis [Internet]. 2016;14(1):45–8.
14. Vargas Castellón DN, Sanchez Salinas SE. Relación de la condición hepática y factores externos en pacientes con dengue. UEB [Internet]. 2022;(9):1-5.
15. Marianneau P, Steffan A-M, Royer C, Drouet M-T, Jaeck D, Kirn A, et al. Infection of primary cultures of human Kupffer cells by dengue virus: No viral progeny synthesis, but cytokine production is evident. J Virol [Internet]. 1999;73(6):5201–6.
16. Kuo C-H, Chiou S-S, Tai D-I, Lan C-K, Liaw Y-F, Chang-Chien C-S. Liver biochemical tests and dengue fever. Am J Trop Med Hyg [Internet]. 1992;47(3):265–70.
17. Krishnamurti C, Nimmannitya S, Nisalak A, Rothwell SW, Cutting MA, Reid TJ, et al. Mechanisms of hemorrhage in dengue without circulatory collapse. Am J Trop Med Hyg [Internet]. 2001;65(6):840–7.
18. Shivbalan S, Anandnathan K, Balasubramanian S, Datta M, Amalraj E. Predictors of spontaneous bleeding in dengue. Indian J Pediatr [Internet]. 2004;71(1):33–6.
19. Alvarez Andrade MEÁ, Sanchez Pérez LM, Ávila Santana K. Choque por dengue y poliserositis en lactantes. Rev Cuba Med Intensiva Emerg [Internet]. 2021;20(4):e855.
20. Díaz-Quijano FA. Predictores de sangrado espontáneo en dengue: una revisión sistemática de la literatura. Invest Clin [Internet].

2008;49(1):111-22.
21. Kularatne SAM, Dalugama C, Rajapakse M, Warnasooriya S, Pathirage M, Ralapanawa U, et al. Blood transfusion in severe dengue infection: a case series. J Med Case Rep [Internet]. 2023;17(1):17.
22. Jagadishkumar K, Jagwani H, Malebennur SK, Seshadri T. Nephrotic syndrome complicated with severe dengue infection in a child. Sudan J Paediatr [Internet]. 2020;20(2):181-5.
23. Wahid SF, Sanusi S, Zawawi MM, Ali RA. A comparison of the pattern of liver involvement in dengue hemorrhagic fever with classic dengue fever. Southeast Asian J Trop Med Public Health [Internet]. 2000;31(2):259-63.
24. Castellanos JE, Esteban P, Panqueba-Salgado J, Benavides-Del-Castillo D, Pastrana V, Acosta G, et al. A case series of severe dengue with neurological presentation in children from a Colombian hyperendemic area. Case Rep Med [Internet]. 2021;2021:6643738.
25. Mitra S, Bhattacharyya R. Hemophagocytic syndrome in severe dengue fever: a rare presentation. Indian J Hematol Blood Transfus [Internet]. 2014;30(1):97-100.
26. Thadchanamoorthy V, Dayasiri K. Dengue fever associated haemophagocytic lymphohistiocytosis: A report of two children. Cureus [Internet]. 2020;12(10):e11232.
27. Munshi A, Alsuraihi A, Balubaid M, Althobaiti M, Althaqafi A. Dengue-induced hemophagocytic lymphohistiocytosis: A case report and literature review. Cureus [Internet]. 2021;13(12):e20172.

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