

## **DENGUE HEMORRHAGIC FEVER COMPLICATED BY MENINGITIS IN A 5-MONTH-OLD INFANT : A CASE REPORT OF RARE NEUROLOGICAL MANIFESTATION**

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### **ABSTRAK**

WHO melaporkan catatan historis lebih dari 14,6 juta kasus *dengue* dan lebih dari 12.000 kematian secara global. Sementara keterlibatan neurologis dalam *dengue* sebelumnya dianggap sebagai kejadian langka, keterlibatan SSP terjadi pada 0,5% hingga 21,2% infeksi virus *dengue*, mulai dari ensefalopati dan ensefalitis hingga meningitis yang jarang dilaporkan. Tantangan dalam diagnosis semakin diperparah oleh fakta bahwa meningitis *dengue* sering muncul sebagai penyakit oligosimtomatik. Studi ini menekankan nilai pemahaman, diagnosis, dan pengelolaan DBD yang rumit oleh meningitis pada bayi berusia 5 bulan dengan keluhan demam disertai kejang dalam 5 hari terakhir. Imunisasi dasarnya tampaknya masih tertinggal dimana imunisasi terakhir adalah pada usia 2 bulan. Pasien tampak sakit sedang dengan kesadaran kompos mentis. Tanda-tanda vital takikardia (nadi 168x/menit). Pemeriksaan leher menunjukkan leher kaku. Kami melakukan beberapa pemeriksaan, seperti laboratorium darah, tes serologi imunoglobulin *dengue*, fungsi ginjal, elektrolit, kalsium, CT scan kepala dengan kontras, tes Mantoux, dan rontgen dada. Pasien didiagnosis meningitis ec DBD. Pasien dirawat bersama dokter anak dan ahli saraf selama 8 hari dan diperbolehkan pulang karena kondisinya membaik.

**Kata kunci** : bayi, demam berdarah *dengue*, meningitis, meningitis terkait DBD, tantangan diagnosis

### **ABSTRACT**

WHO reported a historic record of over 14.6 million *dengue* cases and more than 12,000 deaths globally. While neurological involvement in *dengue* was previously considered a rare occurrence, CNS involvement occurs in 0.5% to 21.2% of *dengue* virus infections, ranging from encephalopathy and encephalitis to the less commonly reported meningitis. The challenge in diagnosis is further compounded by the fact that *dengue* meningitis frequently presents as oligosymptomatic disease. This study emphasizes the value of understanding, diagnosing, and managing DHF complicated by meningitis in 5-month-old infants with complaints of fever accompanied by seizures in the last 5 days. Her basic immunization seems to be still behind; the last immunization was at the age of 2 months. The patient appeared moderately ill with compos mentis consciousness. Vital signs were tachycardic (pulse 168 beats/minute). Neck examination revealed a stiff neck. We performed several tests, such as blood laboratory, *dengue* immunoglobulin serology test, kidney function, electrolytes, calcium, contrast head CT scan, Mantoux test, and chest x-ray. The patient was diagnosed with meningitis ec DHF. The patient was treated together with a pediatrician and a neurologist for 8 days and was allowed to go home because her condition improved.

**Keywords** : *dengue* hemorrhagic fever, meningitis, DHF-related meningitis, infant, diagnosis challenges

### **INTRODUCTION**

*Dengue* hemorrhagic fever (DHF) has emerged as one of the most pressing public health challenges facing the world today, particularly affecting vulnerable populations in tropical and subtropical regions. About half of the people in the globe are now at danger of getting *dengue*. Each year, between 100 and 400 million people get it (WHO, 2025). In 2024, the World Health

Organization (WHO) reported a historic record of over 14.6 million *dengue* cases and more than 12,000 deaths globally, with an estimated 390 million *dengue* infections occurring annually, of which approximately 96 million manifest clinically (WHO, 2025). The disease burden remains disproportionately concentrated in low and middle-income countries, with Southeast Asia, South Asia and Latin America bearing the greatest epidemiological burden (Zhang et al., 2025).

Among the various clinical manifestations of *dengue* infection, the emergence of neurological complications has become increasingly recognized as a serious concern, representing a shift in the clinical paradigm from the traditional hemorrhagic manifestations that dominated earlier descriptions of the disease. While neurological involvement in *dengue* was previously considered a rare occurrence, contemporary studies reveal that central nervous system (CNS) involvement occurs in 0.5% to 21.2% of *dengue* virus infections, with the spectrum of complications ranging from encephalopathy and encephalitis to the less commonly reported meningitis (Shokeen et al., 2018; Pattrakornkul et al., 2022; Domingues et al., 2008; Naderian et al., 2025). This expanding recognition of neurological *dengue* manifestations underscores the need for heightened clinical vigilance and improved diagnostic approaches, particularly in endemic regions where multiple *dengue* serotypes circulate simultaneously.

Indonesia stands at the epicenter of the global *dengue* pandemic, facing an unprecedented surge in *dengue* cases that reflects both the severity of the outbreak and the vulnerability of its population. As of 2024, Indonesia reported 88,593 confirmed DHF cases with 621 deaths (case fatality rate of 0.78%) through mid-year, representing approximately three times the number of cases reported during the corresponding period in 2023. The year 2023 witnessed 114,435 total *dengue* cases nationally with 894 deaths, demonstrating the endemic nature and persistently high burden of this disease in the archipelago (WHO, 2024; Indonesian Ministry of Health, 2024; WHO South-East Asian Region, 2024).

Within Indonesia's highly urbanized centers such as Jakarta, Surabaya, and Bandung, *dengue* transmission remains intense and year-round, with intensification during the rainy season when *Aedes aegypti* mosquito breeding is optimal. The Indonesian health system has documented that *dengue* predominantly affects the pediatric age group, with children representing a substantial proportion of reported cases, and neurological complications have been increasingly documented in hospitalized *dengue* patients (Mikhael et al., 2022; Karyanti, 2011). Multiple risk factors contribute to the escalating *dengue* burden in Indonesia, including high population density, rapid urbanization, inadequate vector control measures, and the simultaneous circulation of multiple *dengue* virus serotypes, particularly *dengue* virus types 2 and 3, which are epidemiologically associated with more severe disease manifestations (Naderian et al., 2025; Pattrakornkul et al., 2022; Karyanti et al., 2011; Soares et al., 2010).

DHF complicated by meningitis represents a particularly challenging clinical entity that warrants special attention due to its rarity and potential for severe morbidity and mortality in the youngest populations. Among pediatric *dengue* patients, neurological complications manifest in diverse forms, with encephalopathy occurring in 53.3% of cases with CNS involvement, followed by encephalitis in 23.3% and myositis in 13.3% (Shokken et al., 2018), whereas meningitis as a primary manifestation is documented in approximately 3.3% of other pediatric *dengue* cases (Ganvir et al., 2023). The pathophysiological mechanisms underlying *dengue* meningitis involve both direct viral neuroinvasion and immune-mediated responses (Naderian et al., 2025), studies have shown that the presence of *dengue* virus in cerebrospinal fluid occurred in 4.3% of cases with suspected CNS involvement, with 85.7% being IgM and 14.3% RNA viral (Bastos et al., 2018). *Dengue* virus serotypes 2 and 3, which are frequently implicated in severe neurological manifestations globally, continue to predominate in endemic regions including Southeast Asia and Indonesia, making the risk of complicated *dengue* presentations persistently high (Soares et al., 2010; Pattrakornkul et al., 2022).

The challenge in diagnosis is further compounded by the fact that *dengue* meningitis frequently presents as oligosymptomatic disease, lacking the typical hemorrhagic manifestations associated with DHF, thereby leading to significant underrecognition and delayed diagnosis in clinical practice (Soares et al., 2010). This study emphasizes the value of understanding, diagnosing, and managing DHF complicated by meningitis in 5-month-old infants.

## METHODS

This study is a case report conducted at K.R.M.T. Wongsonegoro Regional Hospital between May and August 2025. Data collection involved patient history taking, physical examination, and related supporting procedures. Periodic monitoring and evaluation were then conducted during the patient's hospitalization.

## CASE REPORT

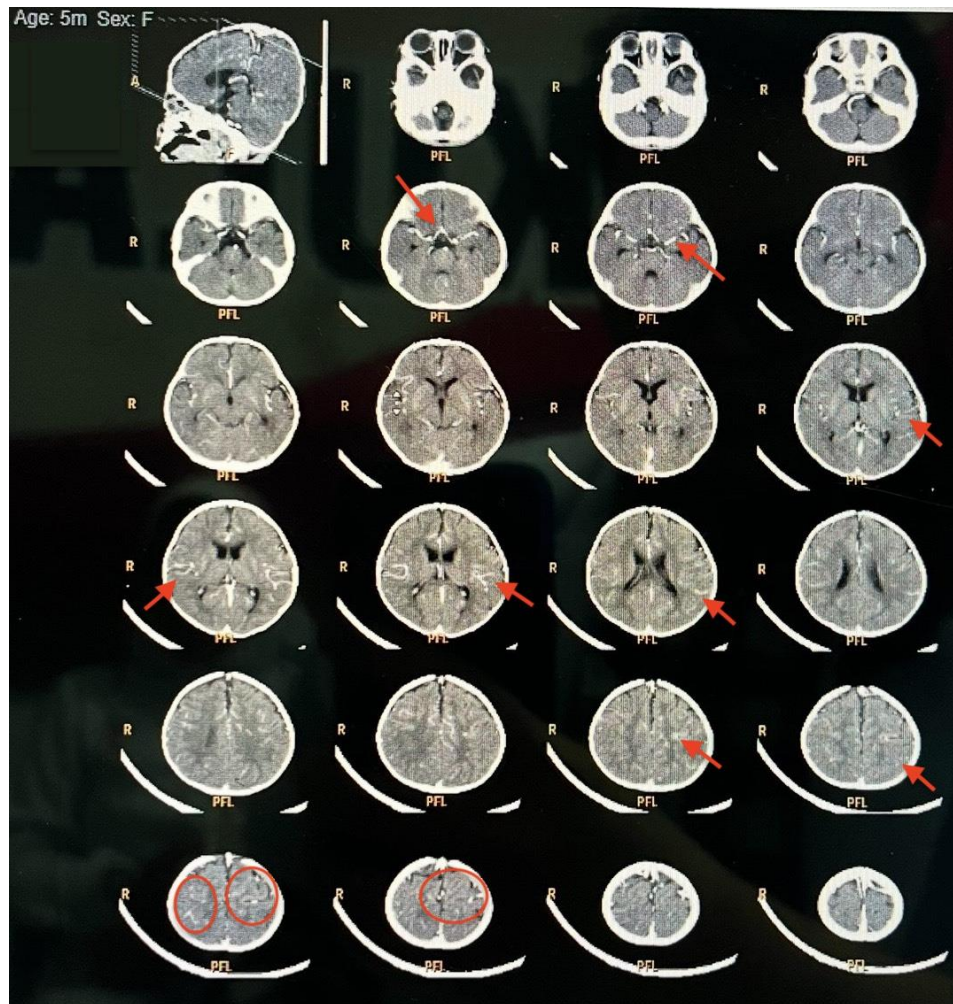
A 5-month-old girl was brought by her mother to the emergency room of Wongsonegoro Regional Hospital with complaints of seizures in the last 5 days. The complaint began when the patient had a fever and was suddenly accompanied by seizures for the first time since 5 days ago. That evening, the patient was given a massage by her parents, and the next day the patient returned with a high fever reaching 39°C. The patient's mother gave her paracetamol, and the fever went down, but suddenly the patient had seizures again. The seizures involved rolling the eyes upwards and occurred more than 10 times per day with a duration of 5 seconds for each seizure. After the seizure, the child regained consciousness. The patient was then taken to the clinic and was advised to go to the hospital. The patient was still willing to breastfeed little by little. The patient's mother also stated that her child had a history of fever 1 month previously for 2 weeks accompanied by a cough and cold but did not experience seizures. However, currently complaints such as cough, cold, vomiting, shortness of breath and weight loss are denied. Red spots, bleeding gums, and nosebleeds are denied. Defecation and urination are within normal limits.

A history of similar complaints was denied. The patient and family denied a history of seizures. The patient's father is an active smoker and has asthma. The patient's older sibling has a history of coughing for 2 weeks without weight loss or fever. The patient is the second of two siblings, born spontaneously vaginally at 38 weeks' gestation. She weighed 2,550 grams. Her mother attended regular antenatal care (ANC) and experienced no complications during pregnancy or delivery. Her most recent immunizations were the first dose of DPT-Hib-Hb and the second dose of polio at 2 months of age. The patient appeared moderately ill with compos mentis consciousness. Vital signs were tachycardic (pulse 168 beats/minute), and other signs were within normal limits. Body weight was 5.5 kg and body length 62 cm. The patient's nutritional status was good with a normal build. Neck examination revealed a stiff neck, and the acral area was warm with a CRT of less than 2 seconds. A Mantoux test was performed, and the result was negative. The chest X-ray results did not show any signs of tuberculosis.

**Table 1. Laboratory Examination Results**

Parameter	ER	Day 1	Day 2	Unit	Reference
Hemoglobin	<b>10.9</b>	11.0	11.1	g/dl	11.7 – 15.5
Hematocrit	<b>31.6</b>	31.9	30.9	%	35 – 47
Platelets	<b>31</b>	30	72	10 <sup>3</sup> /uL	150 – 400
Leukocytes	6.4	3.6	5.8	10 <sup>3</sup> /uL	3.6 – 11.0
Ureum	21.3	-	-	mg/dL	15.0 – 36.0
Creatinine	<b>0.37</b>	-	-	mg/dL	0.5 – 1.1

Blood Glucose	105	-	-	mg/dL	70 – 110
Sodium	135	-	-	mmol/L	135.0 – 147.0
Potassium	5.0	-	-	mmol/L	3.50 – 5.0
Calcium	<b>1.37</b>	-	-	mmol/L	1.00 – 1.15
IgM <i>Dengue</i>	<b>Positive</b>	-	-	-	Negative
IgG <i>Dengue</i>	Negative	-	-	-	Negative
INR	-	0.88	-	-	-
PT control	-	12	-	Sec	-
APTT control	-	27.3	-	sec	-
Patient's APTT	-	31.1	-	Sec	26.0 – 34.0



**Figure 1. CT-Scan Examination Of The Brain with Contrast Found A Picture Of Meningitis Accompanied By Duplex Maxillary and Ethmoidal Sinusitis**

The patient was diagnosed with meningitis ec DHF. Initial treatment was given in the form of an infusion of Ringer's lactate 5cc/kg followed by 3cc/kg. Dexamethasone injection 2x1/3 ampule, diazepam injection 2.5 mg if seizures, valproic acid 2x1 ml, ceftriaxone injection 2x200 mg. During hospitalization, the patient received additional treatment in the form of 75 mg paracetamol infusion/8 hours, 20 mg phenobarbital injection/12 hours, and cotrimazole 2x1/2 cth. After 3 days, the ceftriaxone injection was replaced with a 500 mg meropenem injection/day for 3 days, followed by 2x250 mg and combined with a 75 mg amikacin injection/day. The patient was also given 60cc PRBC transfusions twice (with premedication of 1/3 ampoule of dexamethasone and postmedication of 5 mg furosemide). The patient was

treated together with a pediatrician and a neurologist for 8 days and was allowed to go home because her condition improved.

## DISCUSSION

The presentation of a 5-month-old girl with fever progressing to recurrent seizures within seven days represents a critical diagnostic and clinical challenge in pediatric practice. While febrile seizures remain the most common seizure type in children aged 6 months to 5 years, occurring in approximately 2-5% of this population during febrile illnesses (Xixis, 2024), the constellation of findings in this case—including meningeal rigidity, hypercalcemia, thrombocytopenia, and positive *dengue* immunoglobulin M (IgM) serology—necessitated comprehensive investigation to exclude serious underlying pathology, particularly central nervous system (CNS) infection (Pavone et al., 2022). The neurophysiological basis of fever-induced seizures originates from disruption of the balance between excitatory and inhibitory neurotransmission; fever enhances neuronal excitability through multiple mechanisms including altered ion channel function, particularly hyperpolarization-activated cyclic nucleotide-gated (HCN) and sodium channel (SCN) modifications (Sawires et al., 2022). However, this patient's clinical course—marked by the presence of meningeal signs, imaging evidence of meningitis, and repeated seizure episodes—transcended simple febrile seizure pathophysiology, indicating direct CNS involvement rather than fever-induced lowering of seizure threshold. The initial massage intervention by parents, though culturally contextualized, did not delay recognition of this serious condition, as the mother appropriately sought emergency care following the first seizure episode.

*Dengue* hemorrhagic fever (DHF) represents a severe manifestation of *dengue* virus infection characterized by plasma leakage, coagulopathy, and thrombocytopenia. While DHF classically presents with systemic hemorrhagic manifestations and shock, central nervous system (CNS) involvement through meningitis introduces additional pathophysiological complexity that remains incompletely understood. The development of meningitis in DHF occurs in approximately 5-10% of *dengue* cases with CNS involvement, with seizures representing the most prevalent neurological manifestation in 12.2-34% of *dengue* patients experiencing CNS complications (Ganvir et al., 2024; Bentes et al., 2021). In infants, this complication carries particular significance, as the immature nervous system, developing immune responses, and limited physiologic reserves place these young patients at heightened vulnerability to both direct viral effects and secondary immunopathological damage.

The mechanism by which *dengue* virus crosses the blood-brain barrier and induces CNS pathology operates through three primary pathophysiological pathways: (1) direct viral neuroinvasion with direct viral replication within neural tissue, (2) immune-mediated inflammatory responses secondary to cytokine dysregulation, and (3) indirect metabolic alterations and organ dysfunction affecting CNS homeostasis (Trivedi et al., 2022). In this patient, the detection of positive *dengue* IgM, thrombocytopenia, hypercalcemia, and imaging confirmation of meningitis with concurrent sinusitis strongly suggests direct viral invasion of the meninges combined with secondary inflammatory complications. Recent evidence demonstrates that *dengue* virus enters the CNS during the acute febrile phase, likely facilitated by increased blood-brain barrier permeability caused by cytokine-induced endothelial dysfunction (Naderian et al., 2025).

This patient presented with clinical, laboratory, and imaging findings consistent with *dengue* hemorrhagic fever with meningitis, which according to the 1997 WHO classification criteria would fulfill criteria for DHF grades III or IV when considering the presence of plasma leakage manifestations, thrombocytopenia ( $<40,000/\text{mm}^3$ ), positive hemorrhagic manifestations (as evidenced by hemoconcentration), and, critically, evidence of organ

involvement in the form of CNS complications (Hadinegoro, 2012). The revised 2009 WHO *dengue* classification system, which categorizes cases into *dengue* without warning signs, *dengue* with warning signs, and severe *dengue*, provides enhanced sensitivity in identifying severe cases, with observed sensitivities up to 92% compared to 39% for the 1997 classification (Hadinegoro, 2012). In this case, warning signs justifying hospital admission and intensive management included abdominal pain manifestations in feeding intolerance, clinical fluid accumulation as evidenced by pleural effusion on imaging, altered mental status secondary to meningitis, and rapid hematologic derangements. The presence of encephalitis accompanied by meningitis represents a severe organ involvement criterion, as CNS complications are associated with poorer outcomes and increased mortality when not promptly recognized and managed. Epidemiological data from studies conducted in *dengue*-endemic areas, including Indonesia, demonstrate that DHF in infants carries risks, with studies showing DSS occurring in 20.5% of infected infants and hemoconcentration and thrombocytopenia observed in over 90% of cases (Nguyen et al., 2004). The young age of this patient (5 months) placed her at increased vulnerability, as infants demonstrate different immunological responses to *dengue* compared to older children, with primary *dengue* infection predominating in this age group and characterized by distinct cytokine profiles that may amplify systemic and CNS manifestations.

The initial empiric antibiotic regimen initiated with ceftriaxone (200 mg twice daily), while appropriate for broad coverage of common bacterial meningitis pathogens in the febrile infant, required modification as clinical and laboratory evidence accumulated supporting viral rather than bacterial meningitis etiology (Canadian Paediatric Society, 2020). The standard recommended empiric therapy for suspected bacterial meningitis in children greater than 2 months of age consists of a third-generation cephalosporin (ceftriaxone or cefotaxime) in combination with vancomycin; however, the negative bacterial cultures and positive *dengue* serology guided subsequent therapeutic adjustments in this case (MSD Manuals, 2025). The transition to meropenem (500 mg daily initially, then 2×250 mg) represents appropriate escalation for meningitis management, as carbapenems like meropenem possess advantages in meningitis including superior cerebrospinal fluid penetration compared to other beta-lactams, broad-spectrum activity against both gram-positive and gram-negative organisms, and stability against extended-spectrum and AmpC chromosomal beta-lactamases (Cohen-Wolkowicz et al., 2012).

The clinical judgment demonstrated by the pediatrician and neurologist team in reassessing antimicrobial therapy based on evolving clinical data, laboratory results, and patient response represents evidence-based rational therapeutics. The decision to modify therapy after three days of initial ceftriaxone therapy reflects appropriate responsiveness to clinical deterioration or lack of anticipated improvement, though viral etiology (*dengue* meningitis) would not respond to any antimicrobial agents and required symptomatic supportive care. The mechanisms by which corticosteroids benefit meningitis patients include reduction of inflammation-associated cytokine production, particularly interleukin-1 $\beta$  and tumor necrosis factor- $\alpha$  within cerebrospinal fluid; stabilization of vascular endothelial membranes resulting in decreased vasodilation and vascular permeability; reduction of cerebral edema formation; and redirection of leukocyte migration away from inflammatory sites (Wald, 2025). The 8-day hospitalization involving coordinated management by both pediatric and neurological specialists exemplifies contemporary best practices in complex pediatric critical care, reflecting the multidisciplinary team approach essential for optimizing outcomes in patients with multiple organ system involvement (Stocker et al., 2016).

## CONCLUSION

This case illustrates the complex interplay between viral pathophysiology, systemic inflammation, and CNS involvement in early childhood *dengue* infection. While

simultaneously demonstrating how evidence-based, family-centered, multidisciplinary care can successfully navigate these challenges and achieve positive clinical outcomes.

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