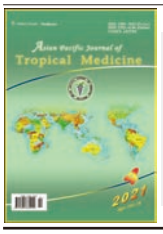

Case Report

Asian Pacific Journal of Tropical Medicine

apjtm.org

doi: 10.4103/1995-7645.312516

Impact Factor: 1.94

Severe dengue associated with aseptic meningitis, acute kidney injury, and sudden sensorineural hearing loss: A case report

Renan GM Diniz[1]✉, Elaine C dos Santos[2], Gabriel CL Chagas[3], Elizabeth F Daher[3]

[1]*Department of Internal Medicine, Faculty of Medicine, Federal University of Ceará, Ceará, Brazil*

[2]*Department of Intensive Care Unit, Fortaleza General Hospital, Fortaleza, Ceará, Brazil*

[3]*Post-Graduation Program in Medical Sciences, Department of Internal Medicine, Federal University of Ceará, Fortaleza, Ceará, Brazil*

ABSTRACT

Rationale: Dengue is the most important human arboviral disease. Neurological manifestations occur rarely in dengue. To the best of our knowledge, there is only one reported case of dengue-associated sudden sensorineural hearing loss (SSNHL) in Brazil untill now.

Patient concerns: A 42-year-old man was presented to the emergency department with unconsciousness and generalized tonic-clonic seizures.

Diagnosis: Dengue-associated aseptic meningitis, acute kidney injury, and SSNHL.

Interventions: The patient was treated with anticonvulsants and thiamine and underwent mechanical ventilation. He received combined ceftriaxone and acyclovir, which were later switched to meropenem, acyclovir and ampicillin empirically until culture results became available. He also required hemodialysis and plasmapheresis sessions and fresh frozen plasma and buffy coat transfusions until definitive diagnosis.

Outcomes: The patient was discharged after improvement of his general condition and of his blood test results, but hearing loss remained. A six-month follow-up visit showed persistent deafness.

Lessons: Dengue should be included in the differential diagnosis of patients from dengue-endemic areas presenting an acute febrile disease with neurological manifestations. To the best of our knowledge, this is the second reported case of dengue-associated SSNHL, suggesting an association between dengue and development of SSNHL.

KEYWORDS: Dengue; Aseptic meningitis; Acute kidney injury; Sensorineural hearing loss; Deafness

1. Introduction

Dengue is the most important arboviral disease affecting humans in terms of morbidity and mortality[1,2]. Usually, it presents as an acute febrile illness[3,4]. Neurological complications are rare, and there is only one report of sudden sensorineural hearing loss (SSNHL)[1,3-6].

In this study, we report a case of aseptic meningitis, acute kidney injury (AKI), and SSNHL in a 42-year-old man with severe dengue.

This case report was approved by the Ethics Committee of Fortaleza General Hospital. The authors obtained written informed consent from the patient.

2. Case report

A 42-year-old man from northeastern Brazil with history of alcoholism and smoking was presented to our emergency department with generalized tonic-clonic seizures. Three days before admission, he had an episode of excessive alcohol intake, followed, on the next day, by fever, severe headache, anorexia, vomiting, watery diarrhea, and abdominal pain. One day before

✉To whom correspondence may be addressed. E-mail: renangomesdiniz@gmail.com

How to cite this article: Diniz RGM, dos Santos EC, Chagas GCL, Daher EF. Severe dengue associated with aseptic meningitis, acute kidney injury, and sudden sensorineural hearing loss: A case report. Asian Pac J Trop Med 2021; 14(4): 187-190.

Article history: Received 2 December 2020 Revision 20 January 2021
Accepted 5 February 2021 Available online 12 April 2021

admission, he suddenly developed dizziness, generalized tonic-clonic seizures, and impaired consciousness.

On arrival, the patient presented Glasgow Coma Scale score of seven, blood pressure of 129/74 mmHg, heart rate of 128 beats/min, and respiratory rate of 24 breaths/min with signs of respiratory distress and bilateral rhonchi at lung bases. During examination, he presented generalized tonic-clonic seizure. Blood glucose was normal, so diazepam was given followed by loading dose of phenytoin and thiamine. He underwent intubation and mechanical ventilation due to refractory status epilepticus. Head CT scan did not show significant abnormalities related to impaired consciousness or status epilepticus. Relevant laboratory investigations are summarized in Table 1. Arterial blood gas analysis showed a pH of 7.25 (reference range: 7.35-7.45), $PaCO_2$ of 28.2 mmHg (reference range: 35-45 mmHg), HCO_3^- of 14 mEq/L (reference range: 22-26 mEq/L), and lactate of 3.8 mmol/L (reference range: 0.5-1.6 mmol/L). In the first six hours, his urine output was 300 mL. Urinalysis revealed numerous red blood cells (RBCs) (reference range: 0-2 cells/hpf), white blood cell (WBC) count of 10-12/hpf (reference range: 0-4/hpf), associated with granular and RBC casts.

As meningoencephalitis was considered as a possible diagnosis, ceftriaxone and acyclovir were prescribed. Lumbar puncture was contraindicated due to thrombocytopenia. Fresh frozen plasma and buffy coat transfusions were prescribed. Acute tubular necrosis due to rhabdomyolysis was suggested, and daily hemodialysis was started due to refractory metabolic acidosis. Serologies for cytomegalovirus, dengue, hepatitis A, B and C viruses, herpes simplex virus, human immunodeficiency virus, leptospirosis, parvovirus, syphilis, and toxoplasmosis were requested.

Due to clinical manifestations and some positive hemolytic markers, thrombotic thrombocytopenic purpura (TTP) was considered a possible diagnosis. Thus, blood sample was collected for ADAMTS-13 activity assay, and plasmapheresis was initiated. On the fourth day, kidney function improved after 3 dialysis sessions, and dialysis was discontinued. On the fifth day, he was transferred to the intensive care unit (ICU) to continue monitoring. Due to persistent fever, ceftriaxone was replaced empirically with meropenem considering its superior cerebrospinal fluid (CSF) activity, and ampicillin was added considering *Listeria monocytogenes* susceptibility. Electroencephalogram showed no epileptiform activity. On the fifth day, his platelet counts increased to 73 000/mm^3 (reference range: 150 000-450 000/mm^3), and lumbar puncture was performed. CSF showed negative Gram stain, glucose of 57 mg/dL (reference range: 40-70 mg/dL), protein of 661.8 mg/dL (reference range: 15-50 mg/dL), RBC count of 320/mm^3 (reference value: 0/mm^3), WBC count of 230/mm^3 (reference range: 0-5/mm^3) with 60% lymphocytes (reference value: 0%), and lactate of 49 mg/dL (reference range: 10-20 mg/dL). On the eighth day, plasmapheresis was discontinued, and extubation was performed due to global improvement. Three days later, he was discharged from ICU.

Previously collected blood, urinary and CSF cultures were all negative. ADAMTS-13 activity assay was 66% (reference range:

Table 1. Hematologic and biochemical findings during hospitalization.

Tests in study	Admission*	Day 4*	Day 11	Reference range
Hemoglobin (g/dL)	11.4	8.1	6.8	M: 13.5-17.8; F: 12-16
Hematocrit (%)	33.6	20.3	21.9	M: 41-54; F: 36-48
Reticulocytes (/mm^3)	51 800	–	–	25 000-100 000
WBCs (/mm^3)	13 200	19 350	7 347	5 000-11 000
Neutrophils (%)	76	75	59	45-70
Lymphocytes (%)	10	6.6	–	20-45
Platelets (/mm^3)	13 310	14 000	243 600	150 000-450 000
INR	1.89	0.88	1.03	$\leqslant$1.2
aPTT ratio	1.85	–	0.97	$\leqslant$1.26
Haptoglobin (mg/dL)	76	–	–	36-195
Coombs test	Negative	–	–	Negative
Sodium (mEq/L)	142	142	153	135-145
Potassium (mEq/L)	4.1	3.6	3.9	3.5-4.5
Calcium (mEq/L)	6.5	9.4	–	8.5-10
Urea (mg/dL)	148	104	32	10-50
Creatinine (mg/dL)	4.6	2.8	0.9	M: 0.7-1.4; F: 0.6-1.2
Total bilirubin (mg/dL)	9.09	0.84	0.32	0.3-1.3
Direct bilirubin (mg/dL)	4.16	0.33	0.15	0.1-0.4
AST (U/L)	830	74	31	12-38
ALT (U/L)	329	64	37	7-41
CK (U/L)	2 273	–	–	M: 38-174; F: 26-140
CRP (mg/L)	171	–	–	0-0.5
LDH (U/L)	878	931	473	240-480

*Peripheral blood smear demonstrated the presence of schistocytes. M: male, F: female, WBCs: white blood cells, INR: prothrombin-time international normalized ratio, aPTT: activated partial thromboplastin time, AST: aspartate aminotransferase, ALT: alanine aminotransferase, CK: creatine kinase, CRP: C-reactive protein, LDH: lactate dehydrogenase. –: test not requested on this day.

⩾70%), not suggestive of TTP. Anti-dengue IgM serology was positive. Anti-CMV IgM, HAV IgM, HBs antigen, HBs IgM, HBc IgM/IgG, HCV IgM, HSV 1 and 2 IgM, fourth-generation antigen/antibody combination HIV-1/2 assay, leptospirosis IgM, parvovirus IgM, toxoplasmosis IgM, and VDRL were negative. So, the diagnosis of dengue was established.

Despite recovery from coma, neurological evaluation was normal, except for partial deafness. Audiometry was performed and revealed moderate to severe SNHL on the right side and hearing loss on the left (Figure 1A). CT of mastoids did not show abnormalities. Family denied deafness before hospitalization.

The patient was discharged after 37 days still with hearing loss, but with important improvement of his general condition and of his blood test results. A six-month follow-up visit showed normal neurologic evaluation, except for persistent deafness (Figure 1B).

3. Discussion

3.1. Aseptic meningitis

Between 0.5% and 5.4% of dengue patients present neurological manifestations, with encephalopathy and encephalitis as the most common[3,5,6]. Meningitis is rare, especially in adults[5,6].

Clinical findings are similar to other causes of aseptic meningitis, including acute onset fever, vomiting, headache, altered consciousness, and nuchal rigidity[4,6].

Lumbar puncture should be done, and CSF analyzed for cell count, glucose and protein concentrations, and detection of viral RNA, NS1 antigen or dengue IgM antibodies[3,5,6]. Specific IgM and IgG antibodies were found in CSF in five to seven days after onset of neurological manifestations[5]. However, absence of IgM detection in CSF does not exclude dengue[3,5].

Our patient presented fever, vomiting, headache, impaired consciousness, and seizures. Neuroimaging study did not reveal structural lesions related to status epilepticus. CSF analysis showed lymphocytic pleocytosis and mild protein increase. CSF analysis for dengue infection was not possible due to laboratory limitations, but with combined clinical history and positive dengue serology, diagnosis of dengue-associated aseptic meningitis was established.

Furthermore, dengue should be a differential diagnosis of acute febrile disease with neurological manifestations in patients from or with recent travel to dengue-endemic areas[3-5].

3.2. Acute kidney injury

Incidence of AKI in patients with dengue varies from 0.9% to 30.7%[7,8]. Etiopathogenesis is multifactorial, including direct cytopathic effects, systemic inflammation, hemodynamic instability, rhabdomyolysis, hemolysis and acute glomerulitis[2].

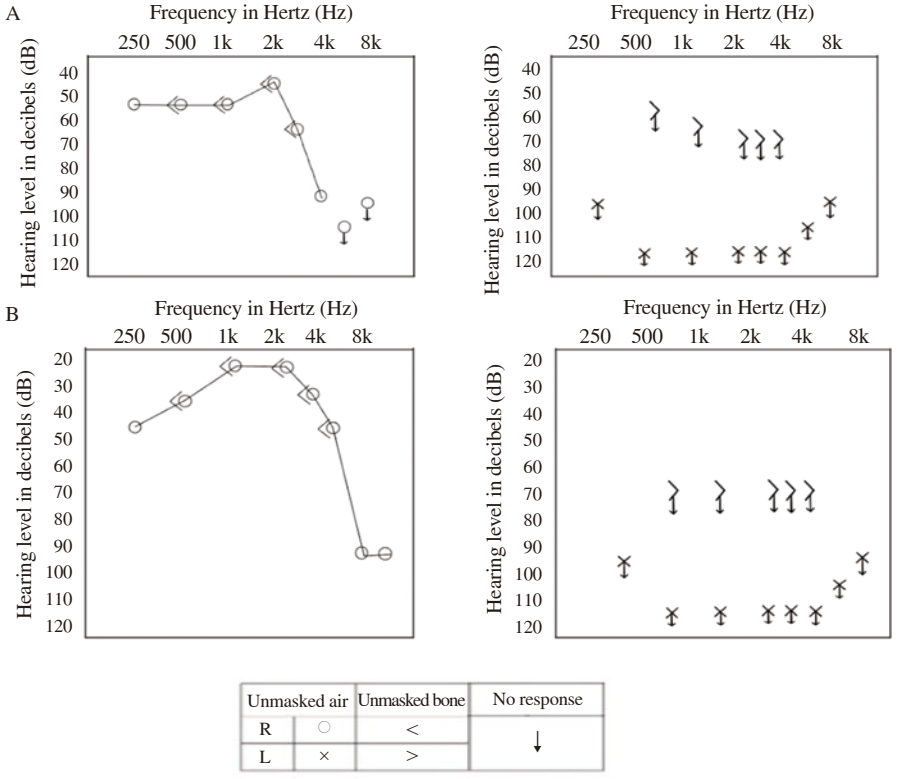

Figure 1. A 42-year-old man with history of alcoholism and smoking presented fever, vomiting, headache, impaired consciousness, and seizures. (A) Pure tone audiometry showed moderate to severe SNHL on the right side and hearing loss on the left. (B) A six-month follow-up pure tone audiometry showed persistent moderate to severe SNHL on the right side and hearing loss on the left.

Dengue-associated rhabdomyolysis might be due to direct viral cytotoxicity or proinflammatory myotoxic cytokines[2]. In this case, the leading factor for development of AKI was likely rhabdomyolysis, secondary to seizures, ethanol intoxication, fever and/or dengue infection. Our patient fully recovered kidney function.

3.3. Sudden sensorineural hearing loss

Sudden sensorineural hearing loss is SNHL that occurs within 72 hours with loss of at least 30 decibels in at least three consecutive frequencies on audiometry, in the absence of prior otological history[1].

Viruses can cause SSNHL by cochleitis or neuritis, viral reactivation within inner ear, or autoimmunity to inner ear antigens[1,9].

Infection by West Nile virus, also a member of the Flaviviridae family, may result in mild to severe bilateral sensorineural hearing loss[9]. Although, there is only one report of a patient with dengue infection that developed SSNHL[1]. In our case, it was not identified other cause for SSNHL besides dengue. Although no cause-effect relationship can be established, our finding supports the association between dengue and development of SSNHL.

Conflict of interest statement

The authors declare that there are no conflicts of interest.

Authors' contributions

RGMD, ECS, GCLC and EFD developed the theoretical formalism. RGMD and ECS followed the patient during hospitalization and acquired the exact data. RGMD, ECS, GCLC and EFD analyzed the data. RGMD, ECS and GCLC wrote the manuscript. GCLC designed the figure. RGMD, ECS, GCLC and EFD contributed to critical revision of the manuscript.

References

[1] Ribeiro B, Guimarães A, Yazawa F, Takara T, de Carvalho G, Zappelini C. Sensorineural hearing loss in hemorrhagic dengue? *Int J Surg Case Rep* 2015; **8**: 38-41. doi:10.1016/j.ijscr.2014.10.057

[2] Oliveira J, Burdmann E. Dengue-associated acute kidney injury. *Clin Kidney J* 2015; **8**(6): 681-685. doi:10.1093/ckj/sfv106

[3] Carod-Artal F, Wichmann O, Farrar J, Gascón J. Neurological complications of dengue virus infection. *Lancet Neurol* 2013; **12**(9): 906-919. doi:10.1016/s1474-4422(13)70150-9

[4] Verma R, Sahy R, Holla V. Neurological manifestations of dengue infection: A review. *J Neurol Sci* 2014; **346**(1-2): 26-34. doi:10.1016/j.jns.2014.08.044

[5] Puccioni-Sohler M, Orsini M, Soares C. Dengue: A new challenge for neurology. *Neurol Int* 2012; **4**(3): 15. doi:10.4081/ni.2012.e15

[6] Li G, Ning Z, Liu Y, Li X. Neurological manifestations of dengue infection. *Front Cell Infect Microbiol* 2017; **7**: 449. doi:10.3389/fcimb.2017.00449

[7] Burdmann EA, Jha V. Acute kidney injury due to tropical infectious diseases and animal venoms: A tale of 2 continents. *Kidney Int* 2017; **91**(5): 1033-1046. doi:10.1016/j.kint.2016.09.051

[8] Prasad N, Novak JE, Patel MR. Kidney diseases associated with parvovirus B19, Hanta, Ebola, and dengue virus infection: A brief review. *Adv Chronic Kidney Dis* 2019; **26**(3): 207-219. doi:10.1053/j.ackd.2019.01.006

[9] Cohen B, Durstenfeld A, Roehm P. Viral causes of hearing loss: A review for hearing health professionals. *Trends Hear* 2014; **18**: 1-17. doi:10.1177/2331216514541361.