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A Case Report on Dengue-Viral Encephalitis with Bilateral Optic Neuropathy Leading to Ophthalmoplegia and Sepsis

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Abstract: ***We present a case of Dengue IgM Antibody-positive viral encephalitis accompanied by bilateral optic neuropathy, ophthalmoplegia, and sepsis, alongside severe thrombocytopenia. MRI findings indicated mild diffuse age-related cerebral atrophy with small vessel ischemic changes and chronic lacunar infarcts, as well as restricted diffusion along the anterior aspect of the intraorbital segments of both optic nerves (with the right being more affected than the left). Visual Evoked Potentials (VEP) revealed abnormalities in the bilateral visual pathway. Subsequently, the patient experienced a gradual loss of complete vision, manifesting only the perception of light, non-reacting pupils, and anisocoria. MRI of the orbit confirmed bilateral optic neuropathy, while alternate-day platelet monitoring demonstrated severe thrombocytopenia concurrent with sepsis.***

Keywords: Encephalopathy, dengue fever, ophthalmoplegia, thrombocytopenia, sepsis, optic neuropathy

1. Background

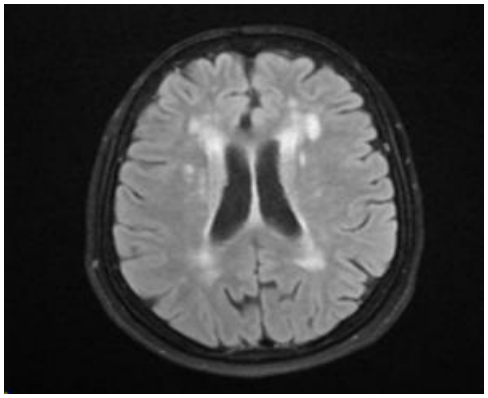
Global burden

The global incidence of dengue has significantly increased in recent decades, with reported cases to the World Health Organization (WHO) rising from 505,430 in 2000 to 5.2 million in 2019 [1]. Despite this, many cases are asymptomatic or mild and go unreported. Additionally, dengue cases are often misdiagnosed as other febrile illnesses. Dengue virus, a single-stranded RNA virus of the Flaviviridae family, causes Dengue fever and dengue haemorrhagic fever. Encephalopathy is a common neurological complication of dengue fever, typically secondary to multisystem derangements such as shock, hepatitis, coagulopathy, and concurrent bacterial infection [2]. DENV-2 and DENV-3 are the strains most frequently associated with neurological complications. The virus's neurotropic nature is thought to lead to encephalitis and central nervous system (CNS) involvement [3]. Sepsis is defined as a life-threatening organ failure resulting from a deregulated host response to infection [4]. Thrombocytopenia, defined as a platelet count <150 G L−1 and classified as severe if <50 G L−1, is the most common haemostatic disorder in the intensive care unit (ICU), with a prevalence of approximately 50% [5, 6, 7]. Notably, platelet count is a component of the SOFA score (Sepsis-related Organ Failure Assessment), used to assess organ dysfunction severity in critically ill patients [5].

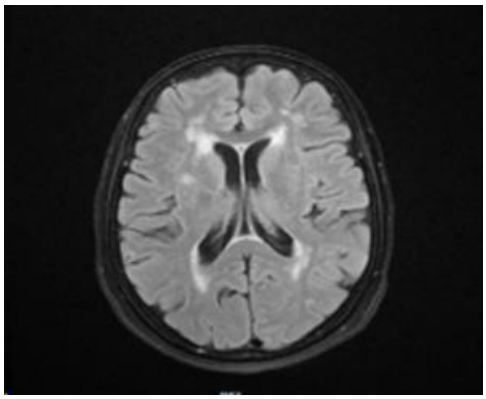
2. Case presentation

A 60-year-old female was admitted to the hospital with complaints of high-grade fever for one week, associated with chills and rigors that lasted for 3-4 days and subsided. She was evaluated outside and found to have thrombocytopenia and leukopenia, but tested negative for dengue. She received management for viral fever, and her symptoms gradually subsided. On September 24, 2023, at 10 pm, she became drowsy, could not recognize her surroundings, and exhibited irrelevant speech. Her past medical history was unremarkable, and on examination, her vitals were stable with a pulse rate of 58/min, blood pressure of 120/80 mmHg, temperature of 98.6°F, and SPO2 of 93% on room air. Cardiovascular examination revealed normal S1S2+ sounds, and respiratory examination revealed bilateral air entry with a soft, non-tender abdomen. Necessary investigations were conducted, and the patient was started on IV antibiotics due to suspicion of viral encephalitis. Initial investigations revealed: hemoglobin (HB) level of 12.9 g/dl, total leukocyte count (TLC) of 6910, platelet count of 1.2 lakh, aspartate aminotransferase (AST) level of 81, and alanine aminotransferase (ALT) level of 45. Dengue IgM testing was positive. A 2D-Echo showed an ejection fraction (EF) of 60% with no regional wall motion abnormalities (RWMA). A CT scan performed for drowsiness revealed mild age-related cerebral atrophy with bilateral periventricular small vessel ischemic changes, and a chronic lacunar infarct in the

right anterior corona radiata. The ventricular system was normal, and the rest of the cerebral parenchyma showed a normal attenuation pattern. Ultrasonography (USG) results were normal. Brain MRI (plain) showed mild diffuse age-related cerebral atrophy with small vessel ischemic changes and chronic lacunar infarcts with restricted diffusion along the anterior aspect of the intra-orbital segments of both optic nerves, more pronounced on the right side.

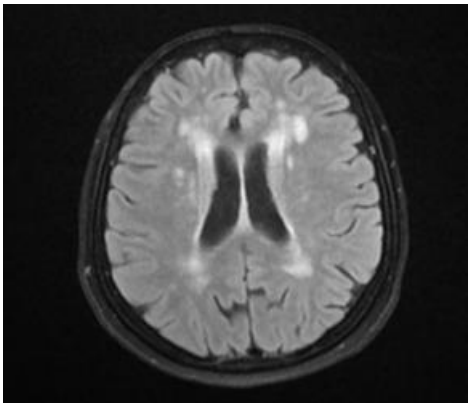


Picture 1

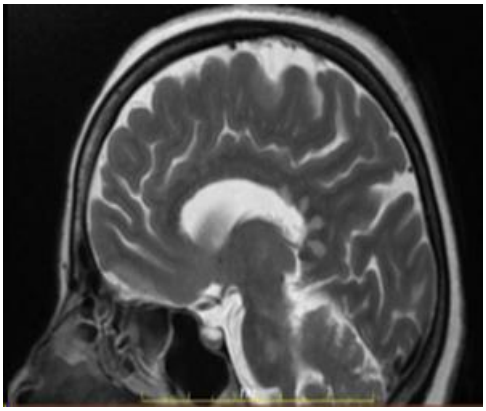


Picture 2

Picture-1, Picture-2 and Picture-3 indicate mild age related cerebral atrophy with bilateral periventricular small vessel ischemic changes, chronic lacunar infarct in right anterior corona radiata.

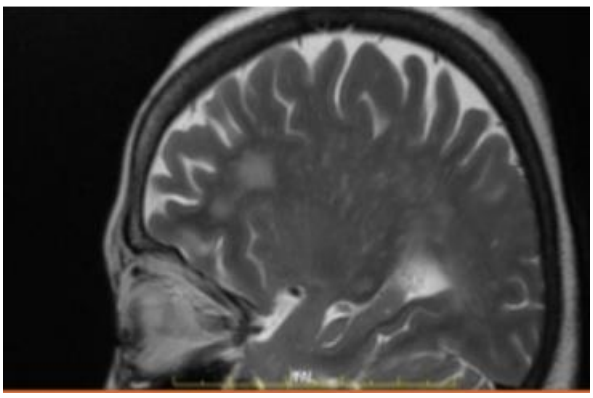


Picture 3

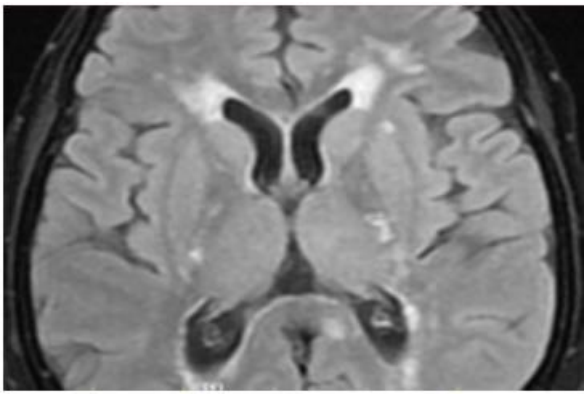


Picture 4

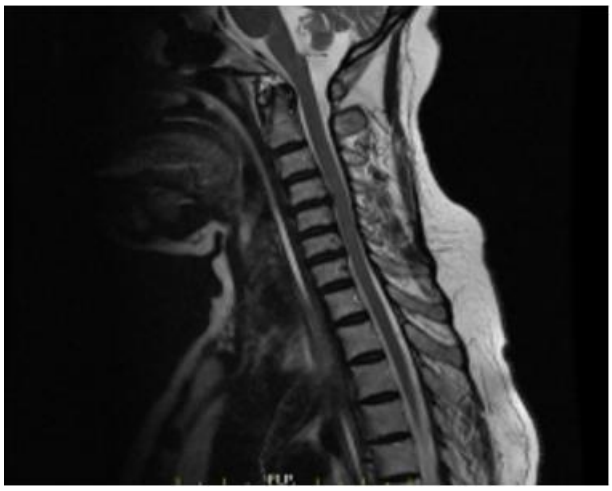
A neurological consultation was sought, and an EEG was recommended, revealing asymmetrical spikes. Treatment with Tab. Brevipil was initiated. CSF analysis was performed, and the patient was prescribed Dexamethasone, Thiamine, and Modalert. Subsequently, the patient, experiencing reduced irritability, reported decreased vision, prompting consultation with an ophthalmologist who recommended VEP, indicating abnormalities in the bilateral visual pathway. On 28/9/23, the patient was transferred to the ward. Over time, the patient progressively lost complete vision, exhibiting only light perception, non-reacting pupils, and anisocoria by 30/9/23. An ophthalmologist was consulted, and OCT was advised, though it could not be conducted due to the patient's condition. MRI of the orbit revealed mild diffuse age-related cerebral atrophy with small ischemic changes and chronic lacunar infarcts. Additionally, multiple small patchy areas of hyperintensity were observed in various brain regions, suggesting a potential viral encephalitis. Notably, restricted diffusion with intra-neural hyperintensity was identified along the intraorbital segments of both optic nerves, without significant enhancement in the post-contrast study. Comparative analysis with a previous MRI dated 25/03/2023 highlighted increased interval involvement of both optic nerves and the onset of multiple discrete hyperintensities in cerebral regions and the brainstem, indicative of ophthalmoplegia.



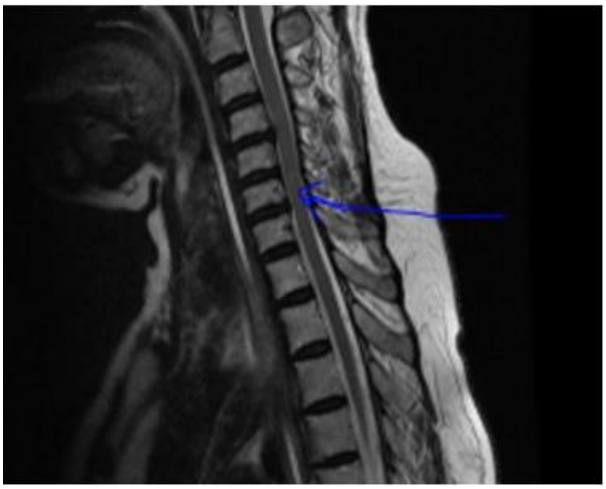
Picture 5: (corona radiata and centrum semiovale)



Picture 6: (Internal capsule)



Picture-7



Picture – 8

Picture – 5,6,7,8 indicates a suboptimal study due to movement artifacts of disc osteophyte complex involving C4/C5 level causing effacement of thecal sac indentation over the ventral surface of the cord with subtle cord signal changes. Disc osteophyte complexes involving C5/C6 and C6/C7 levels caused mild indentation of ventral thecal sac and EEG was carried out which showed asymmetrical spikes.

In view of ophthalmology advice, the bilateral pupil was 3 mm and the patient was obeying all verbal commands. Due to non-cooperation, a torchlight examination was not feasible, but a dilated fundus examination suggested encephalopathy as the likely cause. Later, visual evoked potential (VEP) was performed which showed bilateral visual pathway abnormality. CT brain revealed chronic lacunar infarct and aged-related changes (post viral demyelination). Plasmapheresis (PLEX session) was recommended by physicians due to bilateral optic neuropathy, and the patient underwent four cycles of PLEX while receiving nutrition through a Ryles tube. Additionally, treatment included alternate-day platelet count monitoring due to thrombocytopenia.

On day 25, the patient reported generalized weakness and bedside rashes over the anal region, with a skin tear present in the intergluteal cleft. The patient received bedsore dressing, and a water bed, skin moisturizer, ointments, position changes, and other supportive care were provided, along with physiotherapy sessions. Investigation results from Day 1 to Day 30 revealed episodes of thrombocytopenia (decreased platelet count). On day 17 (1.2), day 19 (80000), and day 20 (72000), values showed severe thrombocytopenia. However, on day 29, the count was within the normal range.

Table 1: Platelet Evaluation Report

S.no	Day	Elevated values	Reference Range
1	Day-1	1.67	1,50,000 – 4, 50,000/ mcl
2	Day-2	1.83	
3	Day-3	2.67	
4	Day-4	3.27	
5	Day-5	3.61	
6	Day-10	2.87	
7	Day-14	1.5	
8	Day-17	1.2 ↓	
9	Day-18	9.9	
10	Day-19	80000 ↓	
11	Day-20	72000 ↓	
12	Day-21	79000 ↓	
13	Day-23	1.24 ↓	
14	Day-26	1.64	
15	Day-29	1.8	

3. Treatment

AQUAPORIN and MOD antibodies were tested and found to be negative. The patient's drowsiness gradually increased, leading to a consultation with a speech therapist as the patient was unable to talk. Mixed RT and oral feed were advised. Neurology consultation resulted in a recommendation for a PLEX trial, following an explanation of the guarded prognosis. Nephrology consultation was sought, and PLEX was performed on 6/10/, 8/10, 10/10, and 13/10. One unit of LDP was transfused on 12/10/23. Subsequently, the patient developed ophthalmoplegia with perception of light. Three units of RDP were transfused on 16/10/23. The neurology team monitored the patient regularly, noting persistent low sensorium and increased drowsiness. Fever spikes prompted an escalation of antibiotic treatment to Meropenem. A grade-II bed sore developed, leading to a consultation with a plastic surgeon, and the recommended advice was followed. The attendee was informed of the patient's poor prognosis, explaining prolonged morbidity and low chances of vision recovery. The patient is being discharged with advice for rehabilitative care, including dietary supplements, tetracycline antibiotics, proton pump inhibitors, beta-lactam antibiotics,

nutritional supplements, vitamins, benzodiazepines, bronchodilators, electrolytes, corticoids, opioid analgesics, type-II diabetic therapy, and other supportive care. Physiotherapy sessions were also conducted as part of the treatment regimen.

4. Discussion

Dengue fever is a mosquito-borne tropical disease caused by the dengue virus [6] Symptoms typically begin after 3 to 14 days of infection [7], and is the leading cause of arthropod-borne viral disease in the world. It is also known as break bone fever due to the severity of muscle spasms and joint pain, dandy fever, or seven-day fever because of the usual duration of symptoms. [8]. Dengue fever is caused by any of four distinct serotypes (DENV 1-4) of single-stranded RNA viruses of the genus Flavivirus. Infection by one serotype results in lifelong immunity to that serotype but not to the other serotype. [9.10.11] Encephalopathy is a very common neurological complication of dengue. Patients with encephalitis typically present with fever and altered sensorium and the MRI brain usually normal in dengue, and thrombocytopenia is a very common clinical manifestation in dengue although there are several hypotheses, the mechanisms involved in thrombocytopenia and bleeding manifestation during DENV infection are not fully understood. By interrupting their function, DENV could directly or indirectly affect bone marrow progenitor cells. [15]

Thrombocytopenia is a common and multifactorial phenomenon occurring during sepsis. The main causes are decreased platelet production, hemodilution, platelets consumption, increased sequestration of platelets in microvessels, and immune-mediated destruction of platelets. The combination of a decrease in the production associated with an increase of platelets consumption and destruction coexists. [16]

Optic neuritis is defined as the inflammation of the optic nerve, which causes sudden painful vision loss or reduced vision in the affected eye. [17, 18] Although most cases of optic neuritis are either idiopathic or associated with multiple sclerosis, post-infectious cause is also known. This is of particular importance in the Asian population where the incidence and prevalence of multiple sclerosis is not as high as in the Western countries. While post-infectious optic neuritis is more common in children. One to three weeks after a symptomatic infection prodrome. [18, 19]

5. Outcome and follow up

Over the 30-day follow-up period of this case, we have concluded that while dengue is not classically a neurotropic virus, recent evidence suggests it can cause direct neuronal injury. Dengue encephalitis should be considered in the differential diagnosis of encephalopathy, and CSF analysis should be performed. As the patient was not stable at the time of discharge and had lost complete vision (ophthalmoplegia), we explained to the attendant the low chances of vision recovery. The patient is being discharged with advice for rehabilitative care and palliative treatment.

Acknowledgements

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