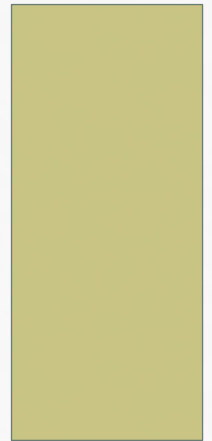


DENGUE FEVER

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NEUROLOGICAL COMPLICATIONS

- The newer classification of neurological involvement with dengue infection aims at disentangling dengue-associated involvement of CNS and eyes, involvement of the PNS, and convalescent or post-dengue immune mediated syndromes

DENGUE ENCEPHALOPATHY

Encephalopathy is the most commonly encountered neurological complication associated with DENV infection.

Dengue encephalopathy may result from systemic infection and may be precipitated by **anoxia**, **cerebral edema**, **hyponatremia**, **prolonged shock**, **systemic hemorrhage**, **acute liver or renal failure**, or the release of toxic substances

DENGUE ENCEPHALOPATHY

- The **CSF profile** is usually normal in cases of dengue encephalopathy.
- **Neuroimaging studies** may be normal or show diffuse cerebral edema

DENGUE ENCEPHALOPATHY

- Recent research suggests that in dengue virus infection, cytokine overproduction results in **immune-mediated endothelial cell damage** which contributes to many of the CNS manifestations

DENGUE ENCEPHALOPATHY

- **Treatment outcome** for patients with dengue encephalopathy is variable and depends on causal/precipitating factors as well as on the extent of medical care

DENGUE ENCEPHALITIS

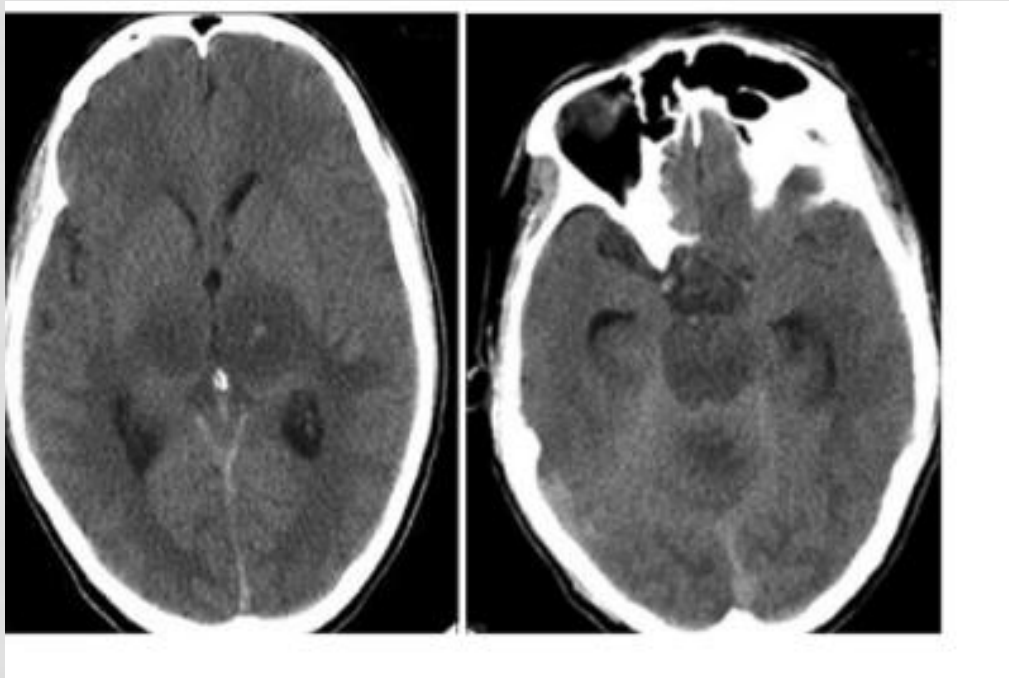
- Reduced levels of consciousness, headache, fever, nausea and vomiting, seizures, focal neurological deficits, and behavioral symptoms may be observed in patients with dengue encephalitis .
- The usual symptoms of dengue fever like rashes, muscular pains, and bleeding are generally not seen in more than 50% of patients with encephalitis.
- DENV-related encephalitic syndrome may be best diagnosed by the combined use of PCR and immunological tests in serum/CSF
- reactive IgM dengue antibody, NS1 antigen or positive dengue PCR on serum and/or CSF

DENGUE ENCEPHALITIS

- Commonly affected regions include the basal ganglia, thalamus, temporal lobes, hippocampus, cerebellum, and cerebral white matter, where T2 sequences may demonstrate hyperintensities
- Rather uncommonly, similar lesions can be found in the brainstem (particularly the substantia nigra) and cerebellum.

DENGUE ENCEPHALITIS

- Non-contrast head CT of a 22-year-old man with DENV encephalitis shows hypodensities in both thalami and brain stem

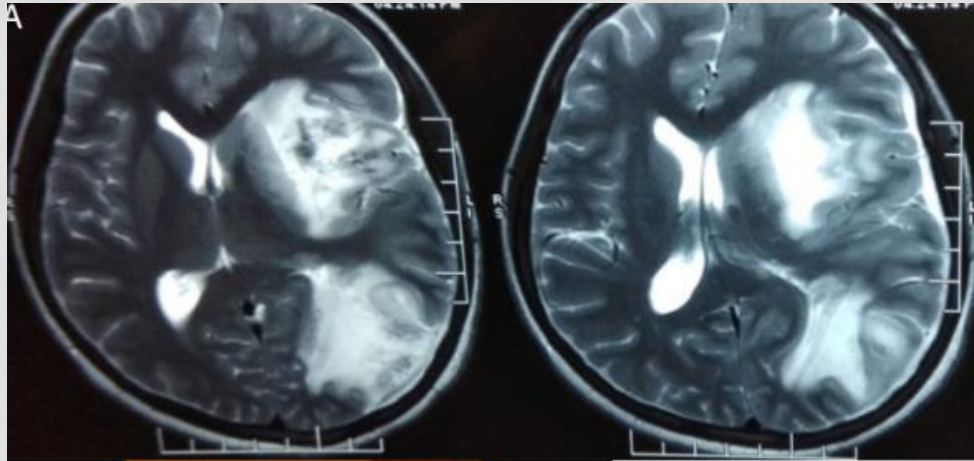


DENGUE-ASSOCIATED STROKE

- A. Ischemic strokes: These may occur as watershed infarctions, **cortical** infarctions, and **lacunar** infarctions.
- B. Hemorrhagic strokes: These may take the form of basal ganglia hemorrhage, lobar hemorrhage (single or multiple), cerebellar hemorrhages (may be bilateral), pontine hemorrhage, subdural hematoma (acute-unilateral or bilateral), pituitary apoplexy (hemorrhagic), and subarachnoid hemorrhages (generally non-aneurysmal

DENGUE-ASSOCIATED STROKE

- Brain MRI (T2sequence) of a 16-year-old adolescent girl with dengue fever who presented with seizures, right hemiplegia, and altered sensorium, showing a large left parietal intracerebral hemorrhage.
- She also complained of visual blurring of the right eye and ophthalmoscopy demonstrated macular edema with star formation

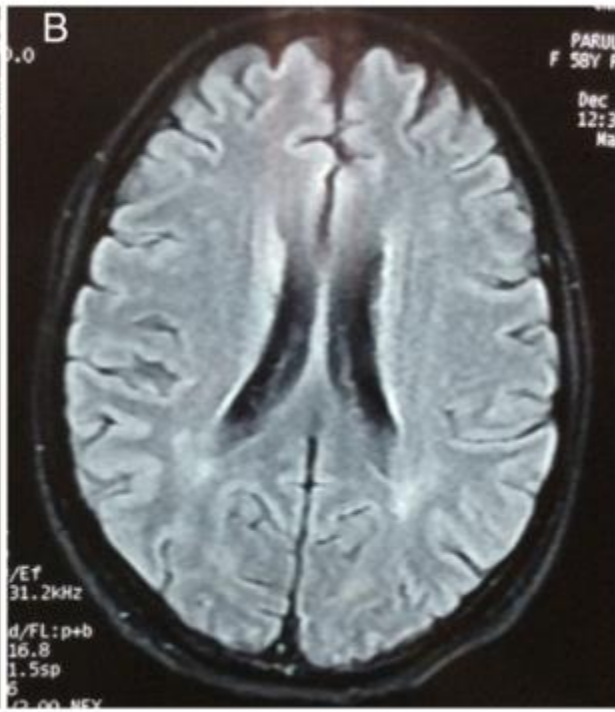
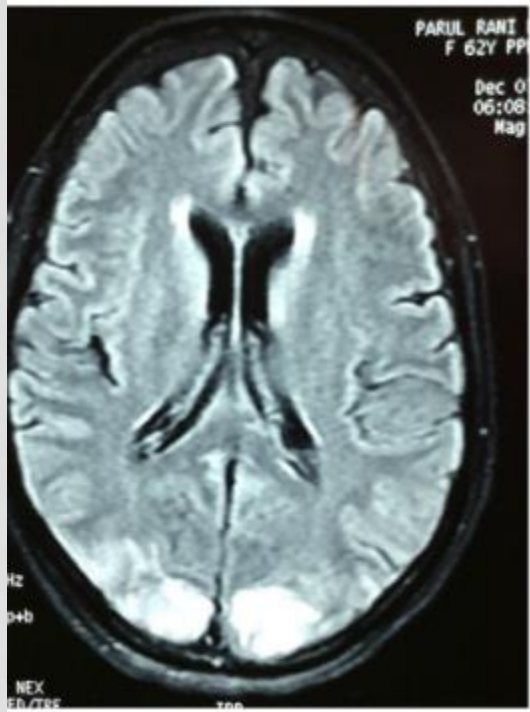


POSTERIOR REVERSIBLE ENCEPHALOPATHY SYNDROME

- **Bilateral cortical visual loss** may be demonstrable in conscious patients or upon regaining consciousness during the recovery stage.
- Its pathogenesis seems to be somewhat different from those encountered in hypertensive emergencies like eclampsia or preeclampsia.
- Posterior reversible encephalopathy syndrome (PRES) associated with dengue virus infection is more of **cytotoxic origin** than vasogenic.

POSTERIOR REVERSIBLE ENCEPHALOPATHY SYNDROME

- Brain MRI (FLAIR sequence) of a 68-year-old woman with dengue fever presented with generalized seizures and altered sensorium.
- On admission, brain MRI showed symmetrical hyperintensities in both occipital regions suggestive of PRES.
- Two weeks after recovery, there was complete resolution of the previously observed signal change



IMMUNE-MEDIATED NEUROLOGICAL SYNDROMES

- Mononeuropathies
- GBS
- brachial neuritis
- transverse myelitis
- ADEM
- acute cerebellitis
- myoclonus syndrome
- Parkinsonism

MONONEUROPATHIES

- Involvement of cranial nerves following dengue fever includes:
 - optic neuritis
 - oculometers nerve palsy
 - isolated sixth nerve palsy
 - isolated Bell's palsy
 - long thoracic neuropathy
 - isolated phrenic nerve palsy
- **Diagnosis** :is usually one of exclusion
- Treatment mostly supportive.
- **Corticosteroids** may be helpful if prescribed early in the course

GILLIAN BARER SYNDROME AND VARIANTS

- GBS may occur early in the course of the illness or may be delayed.
- The exact pathogenetic mechanism is unclear, but it is highly likely that this is an immune-mediated disorder, as immunoglobulin evoked by dengue infection cross-react with peripheral nerve components, which share cross-reactive epitopes

ACUTE TRANSVERSE MYELITIS

- It can occur **during or after the infection**.
- **Long segment involvement** is the rule.
- Post-infectious immune-mediated myelitis usually arises within **1–2 weeks after the onset of initial symptoms**, whereas parainfectious myelitis can take place within the first week of infection. Diagnostic confirmation demonstrates signal changes and spinal cord swelling on MR imaging of the spinal cord. Intrathecal synthesis of dengue virus-specific IgG antibodies in the CSF has been detected as well as isolation of viral RNA can be made

ACUTE DISSEMINATED ENCEPHALOMYELITIS

- ADEM may occur **during the convalescence phase** following DENV infection and DHF
- Presenting symptoms often include seizures, altered sensorium, and focal neurological deficits
- Such symptoms generally occur after remission of the febrile period.
- Mild **CSF pleocytosis** and **moderate rise in protein** concentration may be present in the CSF.
- Brain MRI studies detect white matter lesions on T2-weighted and FLAIR images in the centrum semiovale, corona radiata, corpus callosum, and thalamus.
- Spinal cord signal alterations can be detected mostly in the thoracic and cervical segments

OCULAR MANIFESTATIONS

- Maculopathy
- subconjunctival hemorrhages,
- uveitis,
- vitritis,
- retinal hemorrhages,
- retinal venular widening,
- higher retinal vascular dimension,
- retinal vascular sheathing,
- retinal pigment epithelium mottling,

- acute macular neuroretinopathy
- intra-retinal edema
- cotton wool spots
- Roth's spot
- retinal detachment
- Retinochoroiditis
- Neuroretinitis
- choroidal effusions
- choroidal neovascularization
- optic disc swelling and neuritis
- oculomotor nerve palsy,
- panophthalmitis

OCULAR MANIFESTATIONS

- symptoms of ocular involvement are suggested by visual loss, ocular pain, redness, impaired color vision, diplopia, eye flashes and floaters, and photophobia.
- Lesions located in the peripheral retina may be asymptomatic

OCULAR MANIFESTATIONS

- Most dengue-related ocular conditions **resolve spontaneously**. **Steroids** may be helpful when an autoimmune mechanism is suspected, but they should be avoided in the stage of acute viremia,

DENGUE-ASSOCIATED HYPOKALEMIC PARALYSIS

- Development of hypokalemic paralysis can be suspected in patients presenting with acute onset of flaccid quadriplegia **without any cranial nerve palsy** and without **any sphincteric compromise**.
- Demonstration of hypokalaemia is confirmatory.

DENGUE-ASSOCIATED HYPOKALEMIC PARALYSIS

- A serum potassium level of 3 mmol/liter or below would suggest the diagnosis of hypokalemic paralysis.
- The onset of weakness generally occurs on an average between the 2nd and 5th day of fever, developing over a period of 4–24 h.
- In most patients, muscle stretch reflexes are usually absent or decreased

DENGUE-ASSOCIATED HYPOKALEMIC PARALYSIS

- DENV-associated hypokalemic paralysis responds to low doses of potassium supplementation with rapid recovery without any residual deficits

DENGUE-ASSOCIATED HYPOKALEMIC PARALYSIS

- a) **Excess use of intravenous fluid**, especially lactate containing solutions, may promote metabolic alkalosis, which results in an intracellular shift of potassium, thereby lowering the serum level of potassium.
- b) **Due to redistribution of potassium** within cells an extracellular fluid as a systemic effect of the infection
- c) **Transient renal tubular abnormalities** lead to increase urinary potassium excretion.
- d) **Stress-induced catecholamine release** induces cellular uptake of potassium resulting in hypokalemia.

MYOSITIS

- Dengue-associated myositis can be of varying severity, ranging from **self-limiting mild muscle** weakness to **severe dengue myositis**, resulting in quadriparesis and respiratory insufficiency
- Concomitant myocarditis may complicate management.
- The proposed mechanisms comprise direct muscular invasion by the DENV and immune mediated destruction of muscle fibers

MYOSITIS

- **EMG** findings are consistent with a **myopathic pattern**
- Dengue myositis is considered a relatively benign and self-limiting disease among pediatric patients. In adult patients, dengue myositis is often more severe, even leading to severe rhabdomyolysis.
- A **persistent form of severe myositis**, but responsive to corticosteroids, has been described

RHABDOMYOLYSIS

- Dengue-induced rhabdomyolysis likely results from **cytokine-mediated damage** to muscle cells. .
Raised levels of cytokines result in an **increase in intracellular free calcium**, resulting from depletion of adenosine triphosphate (**ATP**) and/or by direct injury and disruption of the plasma membrane. Increased intracellular calcium level is injurious to muscle cells through **activation of proteases**, **mitochondrial abnormalities**, and excessive production of reactive oxygen species all these chemical reactions ultimately result in muscle cell death
- Rhabdomyolysis may cause acute kidney injury (AKI) and life-threatening electrolyte disturbances

MYALGIAS

- Muscle pain, tenderness, and mild muscle swelling are the characteristic features, noted **during the early phase** of the illness.
- The **pain** commonly affects the **back and proximal limb muscles**, causing difficulty in walking in the absence of any weakness. It is likely that direct viral invasion of muscles occurs,
- Myalgias are often transient and **self-limiting**
- **Electromyography** (EMG) is usually normal

THANK YOU