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Case Report

Successful Management of Acute Disseminated Encephalomyelitis Following Dengue Infection: A Rare Case Report

Lahari Samudrala[1*], Bhanu Pratap Singh[2], Rajya laxmi Papasani[2], Tharun Bashaboina[2], Ramarao Tadikonda[3]

[1]Department of PharmD, CMR College of Pharmacy, Hyderabad, India.

[2]CMR College of Pharmacy, Hyderabad, India.

*Corresponding author: Samudrala.lahari@gmail.com

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ABSTRACT

This case report presents the clinical course of an 18-year-old patient who presented with a constellation of symptoms including fever, vomiting, diplopia, blurred vision, and progressive alteration of sensorium. Laboratory investigations revealed a positive dengue NS1 antigen test. Through a meticulous differential diagnosis process, acute disseminated encephalomyelitis (ADEM) was established as the most probable etiology based on clinical presentation and neuroimaging findings. The therapeutic regimen included intravenous and oral corticosteroids, adjunctive antibiotic therapy, intravenous immunoglobulin, and antiepileptic medication. The patient demonstrated a favorable clinical trajectory with significant improvement observed on the 19th day of hospitalization. This case report underscores the intricate diagnostic and therapeutic considerations crucial for achieving optimal patient outcomes in ADEM.

Keywords: Acute disseminated encephalomyelitis, Neurological complications, Intravenous immunoglobulin, Corticosteroids, Altered mental status, Patient outcomes.

INTRODUCTION

Acute disseminated encephalomyelitis (ADEM) represents an uncommon immune-mediated inflammatory condition characterized by demyelination within the central nervous system. It frequently follows viral infections or immunizations. In light of the persisting COVID-19 pandemic and the widespread administration of vaccines, the prevalence of ADEM is likely to rise[1]. ADEM is slightly more frequently observed in male children. It is a rare neurological disorder, with its incidence varying between 0.07 and 0.6 per 100,000 individuals, as reported in population-based studies[2]. ADEM may arise during the acute or post-infectious phase of dengue fever. An immune response triggered by molecular mimicry targets myelin, resulting in demyelination of the brain's white matter, spinal cord, or both. Typically, ADEM presents as a multifocal, monophasic condition characterized by altered mental status, seizures, and focal neurological deficits. According to one meta-analysis, the onset of post-dengue ADEM has been observed between 3 and 19 days following dengue infection.[3] Dengue virus serotypes 2 & 3 are primarily linked to neurological complications, including encephalopathy, meningitis, encephalitis, stroke, and immune-mediated conditions such as ADEM.[4] The recovery period for dengue-associated ADEM typically spans one to four weeks, consistent with the general recovery timeline for ADEM. However, some cases have reported recovery as early as three days.[5] This case report aims to highlight the neurological and hematological manifestations of ADEM, along with its successful resolution through meticulous management involving corticosteroids and immunoglobulin therapy over a 19-day period.

Case Presentation

An 18-year-old patient with no comorbidities presented with chief complaints of high-grade, intermittent fever not associated with chills or rigors, and vomiting that worsened with food intake. The vomiting was non-projectile, non-bilious, and not mixed with blood, persisting for one week. The patient also reported a history of double vision and blurring of vision for three days, followed by altered sensorium for two days, characterized by decreased responsiveness to verbal commands, failure to recognize attendants, and disorientation to time, place, and person. There was no history of seizures, trauma, chest pain, palpitations, or bleeding manifestations. On examination, the patient was conscious but incoherent and afebrile. Vitals, pupils, and plantar reflexes were normal, but a downward gaze of the eyes was noted. The Glasgow coma scale (GCS) was assessed as E2V2M5. Kernig's sign was negative, and no neck stiffness was observed. Urine output was not quantified.

Viral markers, complete blood picture, renal function tests, and liver function tests were ordered. Results revealed a positive dengue NS1 antigen, elevated alanine transaminase (837 U/L), and aspartate transaminase (595 U/L). Based on clinical findings and laboratory reports, the patient was provisionally diagnosed with dengue NS1 positive with viral encephalitis, transaminitis, and

thrombocytopenia. Initial treatment included injection of acyclovir 600 mg in 100 mL normal saline thrice daily, capsule doxycycline 100 mg twice daily, pantoprazole 40 mg once daily, and ondansetron 4 mg twice daily. The patient was fed through a Ryle tube with 100 mL of milk or water every two hours in a propped-up position.

On the second day of admission, the treatment plan was updated to include intravenous doxycycline 100 mg twice daily, injection of dexamethasone 10 mg four times daily, injection of mannitol 20% 100 mL four times daily, tablet S-adenosylmethionine 400 mg three times daily, and tablet calcium 500 mg once daily, along with continued IV fluids. The patient exhibited no fever spikes, bleeding manifestations, or seizures. An MRI scan was ordered, and the patient was referred to neurology for further evaluation. Neurological examination revealed the patient was conscious but drowsy, with no significant reflex lag in the pupils. The patient moved all four limbs but was uncooperative during extraocular movement testing. MRI findings showed subcortical, brainstem, and cerebellar hyperintensities. The neurologist prescribed an injection of methylprednisolone 1 g once daily for five days, followed by a tablet of prednisolone 40 mg daily, and an injection of levetiracetam 500 mg twice daily. Antibiotic coverage, physiotherapy, back care, and bladder care were also advised.

On the fourth day, the patient exhibited moderate impairment of consciousness with spontaneous eye opening, inappropriate verbal responses, and localization of pain (E4V3M5). There was no improvement in sensorium, but vitals were stable, and blood sugar was 144 mg/dL. Laboratory findings indicated recovery from transaminitis and thrombocytopenia as shown in the Table 1. On the fifth day, Babinski's sign was elicited as positive. Treatment continued with methylprednisolone, doxycycline, pantoprazole, ondansetron, levetiracetam, and S-adenosylmethionine, along with back, bowel, and bladder care. By the sixth day, the patient showed improved sensorium, was able to obey some commands, and had no fever spikes, bleeding manifestations, or seizure activity. Intravenous medications were transitioned to oral forms, including tablet prednisolone 40 mg once daily, capsule doxycycline 100 mg twice daily, and syrup oral glycerol (10 mL diluted in a glass of water) thrice daily. The clinical and laboratory findings at this stage suggested a suspected diagnosis of ADEM secondary to viral infection, with transaminitis, thrombocytopenia and Herniation of cerebellar tonsils.

On the ninth day, the patient was conscious and irritable, with full recovery from thrombocytopenia and transaminitis but no significant improvement in sensorium. On the tenth day, the vomiting subsided, and the patient was arousable and febrile. Tablet acetaminophen 650 mg was added thrice daily, and a urine output of 1.5 liters per day was documented. The same course of treatment was continued for another seven days. A follow-up neurological consultation based on laboratory reports, MRI findings, and clinical symptoms confirmed a diagnosis consistent with ADEM/dengue encephalitis. No lesions involving the temporal lobe, thalamus, or basal ganglia were observed to suggest limbic encephalitis. The neurologist recommended continuing the tablet of prednisolone 40 mg daily and adding a tablet of risperidone 2 mg once daily, a tablet of trihexyphenidyl 2 mg once daily, and an injection of haloperidol (half ampule SOS), along with intravenous immunoglobulin (IVIG) 400 mg/kg body weight for five days. The treatment regimen, including IV Fluids, IVIG, levetiracetam 500 mg twice daily, pantoprazole 40 mg daily, multivitamin injections, oral glycerol, and risperidone, was continued.

By the 19th day, the patient showed signs of recovery with normal vitals and a negative Babinski sign. The patient has been discharged

Table 1: Laboratory findings

Parameters	*Day 1*	*Day 2*	*Day 3*	*Day 6*	*Day 7*	*Day 10*	*Day 14*
WBC (10^9/L)	7.8	10.57	10.86	13	12.35	16.33	7.74
RBC (10^{12}/L)	-	-	5.96	-	5.80	5.60	4.98
Hb (g/dL)	10.8	10.9	10.3	10.3	10.5	10.2	9.3
PLT (10^9/L)	77	89	241	311	313	268	240
HCT (%)	37.2	37	35.6	-	36.9	36.1	32
MCV (fL)	61.6	60	59.7	-	63.6	64.5	64.3
$Na^+/K^+/ Cl^-$ (mEq/L)	136/4.1/98	-	130/4.3/94	-	127/4/90	125/3.6/88	134/3.2/99
Urea (mg/dL)	11	37	29	37	28	25	16
Sr. Creatinine (mg/dL)	0.6	0.75	0.66	0.4	0.55	0.47	0.48
Total Bilirubin (mg %)	0.69	0.9	0.9	0.82	0.70	0.37	0.37
AST (U/L)	595	396	162	123	42	20	38
ALT (U/L)	837	412	214	99	88	66	61
ALP (U/L)	71	79	79	52	97	141	170
Albumin (g/dL)	2.9	3.6	3.6	3.9	3.53	3.73	3.59
GGT (U/L)	61	-	-	-	-	-	-

Note: *WBC- White blood cells (4–11 10^9/L), RBC- Red blood cells (3.50–5.50 10^{12}/L), Hb- Hemoglobin (12–13 mg/dL), PLT- Platelet count (150–450 10^9/L), HCT- Hematocrit (37–54%), MCV- Mean cell hemoglobin (80–100 fL), Na^+- Sodium (136–145 mEq/L), K^+- Potassium (3.6–5.1 mEq/L), Cl^-Chlorine (98–107 mEq/L), Urea (15–40 mg/dL), Serum Creatinine (0.70–1.3 mEq/L), Direct Bilirubin (0.2–1.1 mg%), Direct Bilirubin (0.03-0.18 mg/dL), AST- Aspartate Aminotransferase (5–35 U/L), ALT- Alanine Aminotransferase (7–40), ALP- Alkaline Phosphatase (28–111 U/L), Albumin (3.5–5.7 g/dL), Total Protein (6–8g/dL), Globulin (2–3.5 g/dL), GGT- Gamma-Glutamyl Transferase(5–36 U/L).*

on a tablet of prednisolone 30 mg once daily, a tablet of multivitamin once daily, and a tablet of levetiracetam 500 mg twice daily, with a follow-up advised after two weeks. On follow-up, the patient was clinically stable and improving.

MRI of the brain revealed patchy cortical and subcortical T2 FLAIR hyper-intensities involving the bilateral periventricular white matter, right thalamus, and cerebral peduncles, along with diffuse hyper-intensities in the vermis and bilateral cerebellar peduncles showing diffuse restrictions. Mild compression of the fourth ventricle with resultant mild supra-tentorial hydrocephalus and slight descent of the cerebellar tonsils by approximately 6 mm was noted. These findings are suggestive of viral or dengue encephalitis, with a probable diagnosis of Acute Disseminated Encephalomyelitis. Cerebrospinal fluid analysis on the 14th day revealed 1-cell/mm^3 with 100% lymphocytes and no bacterial growth on culture. Ultrasound of the abdomen showed bilateral trace pleural effusion and mild splenomegaly, while the 2D echocardiogram was a normal study.

DISCUSSION

Acute disseminated encephalomyelitis is an autoimmune disorder characterized by the destruction of myelin within the brain and spinal cord. Typically monophasic in nature, it manifests as an acute and swiftly progressive condition involving multifocal neurological impairments. A significant proportion of cases are linked to antecedent viral or bacterial infections. Pathogens such as *Mycoplasma pneumoniae*, HIV, influenza, Epstein-Barr virus, herpes simplex virus, human herpesvirus-6, smallpox, measles, rubella, mumps, and varicella have been identified as potential triggers. Additionally, a correlation exists between ADEM and prior immunization, with post-vaccination cases historically comprising approximately 5% of reported instances [6]. Observations provide credence to the hypothesis that COVID-19 may serve as a viral catalyst for the onset of ADEM [7]. An extensive compilation of case reports and case series has posited a plausible connection between ADEM and immunization against COVID-19.[8] The onset of neurological symptoms in ADEM typically follows the febrile phase, with manifestations often emerging 1 to 3 weeks after the triggering event, whether an infection or vaccination.[9]

The clinical presentation of this condition typically commences with a prodromal phase characterized by a constellation of nonspecific symptoms, including pyrexia, cephalalgia, malaise, nausea, and emesis. Subsequently, an acute phase ensues, marked by the emergence of encephalopathy. This encephalopathic state manifests as aberrant behavioral patterns such as irritability and confusion & alterations in the level of consciousness, ranging from lethargy and stupor to coma. In this case patient experienced high-grade fever along with persisting vomiting for 1 week. Concomitantly, the patient may exhibit neurological deficits, either multifocal or focal in nature, contingent upon the specific regions of the central nervous system (CNS) affected by the demyelinating process. Involvement of the occipital lobe and the visual cortex can engender a spectrum of visual disturbances, encompassing homonymous hemianopsia and progressing to cortical blindness. Furthermore, dysfunction within the associative cortical regions may result in the emergence of aphasia, alexia, agraphia, or acalculia. In this instance, the patient presented with a three-day history of diplopia and blurred vision, followed by two days of altered sensorium, marked by diminished responsiveness to verbal cues, inability to recognize caregivers, and disorientation to time, place, and identity.

Finally, if the pathological process impinges upon the motor cortex, the clinical picture may be further complicated by the emergence of pyramidal tract signs, including muscular weakness, paresis or paraplegia, hyperreflexia, spasticity, and the presence of the Babinski reflex.[10]

The predominant hypothesis suggests that ADEM arises from a molecular mimicry response, wherein structural similarities between the initial immunogenic pathogen and the host's myelin proteins trigger an autoimmune reaction. This process is initiated during post-infection immune surveillance, as homologous myelin basic proteins are mistakenly identified as foreign, activating the autoimmune cascade. An alternative, plausible explanation proposes a direct cytotoxic assault on the CNS by pre-existing encephalitogenic monoclonal T-cells, which are activated by the inflammatory response resulting from the primary pathogen infection. In the case of post-dengue ADEM, most instances failed to detect the dengue virus in cerebrospinal fluid (CSF), lending further support to the immune-mediated theory of ADEM. CSF examination may uncover distinctive abnormalities suggestive of ADEM, such as pleocytosis and heightened protein concentrations, which serve as potential diagnostic markers.[11]

The diagnosis of ADEM relies primarily on clinical assessment and corroboration through neuroimaging techniques. A significant challenge in the definitive diagnosis of ADEM stems from the absence of specific biomarkers. This necessitates ongoing research endeavors aimed at identifying definitive biological markers for this condition. Given the presence of numerous conditions that can mimic the clinical presentation of ADEM, a meticulous differential diagnostic process is imperative. Consequently, the diagnosis of ADEM is typically established through a process of exclusion, whereby other potential etiologies are systematically ruled out. A comprehensive evaluation excluded numerous differential diagnoses in confirming ADEM. Kernig's signs, neck stiffness, seizures, trauma, chest discomfort, palpitations, or bleeding tendencies were absent in this patient. Neuroimaging further demonstrated no involvement of the temporal lobe, thalamus, or basal ganglia, thereby conclusively excluding the possibility of limbic encephalitis. Within the diagnostic workup of ADEM, craniospinal magnetic resonance imaging (MRI) assumes a pivotal role. This advanced imaging technique serves not only to establish the diagnosis of ADEM but also to effectively differentiate it from other demyelinating disorders of the CNS, such as Neuromyelitis optica spectrum disorder, multiple sclerosis, and neuromyelitis optica, which may exhibit overlapping clinical presentations. Characteristic neuroimaging findings in ADEM typically include the presence of hyperintense lesions on T2-weighted and fluid-attenuated inversion recovery (FLAIR) sequences, predominantly involving subcortical and deep white matter structures, as well as the spinal cord and brainstem.[10]

The cornerstone of acute ADEM management involves high-dose corticosteroids, typically methylprednisolone administered at 30 mg/kg/day for 3 to 5 days, with a maximum daily dose of 1000 mg. A

gradual oral steroid taper over a period exceeding 3 weeks is believed to reduce the risk of early recurrence, with a 4 to 6-week taper being standard practice. In refractory cases, intravenous immunoglobulin (IVIG) and plasma exchange have been employed with varying degrees of success. In this case study injection of methylprednisolone 1 g once daily for 5 days, IVIG 400 mg/kg body weight for 5 days, injection of levetiracetam 500 mg twice daily and then tapered with oral corticosteroid by tablet prednisolone 30 mg daily. Then by the 19th day, the patient demonstrated notable improvement and was showing progressive enhancement.

Given that ADEM is predominantly monophasic, acute treatment is typically the sole intervention required in most instances. Follow-up imaging is generally conducted at 3 months to establish a baseline for potential future episodes of recurrent demyelination. The detection of MOG antibodies enhances our ability to prognosticate the likelihood of recurrent attacks. Furthermore, the presence or absence of MOG antibodies is increasingly influencing management approaches. Recent evidence indicates that in MOG-positive patients experiencing recurrent demyelination, immunosuppressive therapy may significantly reduce the rate of relapses.

Individuals with monophasic ADEM are generally expected to achieve favorable outcomes, with complete recovery commonly occurring within a few weeks or months. Nevertheless, a small subset of patients may endure persistent motor deficits or develop epilepsy. Alarmingly, recent data has revealed an acute mortality rate of up to 3% in pediatric patients and over 10% in adults in the past decade.[12]

A significant proportion of children afflicted with ADEM exhibit a favorable response to high-dose corticosteroid therapy alone, rendering the administration of additional immunomodulatory agents potentially unnecessary. However, the presence of severe neurological sequelae, such as ambulatory dysfunction, profound visual impairment, persistent cognitive disturbances, or refractory seizures, may necessitate the implementation of adjunctive therapeutic interventions. These may encompass the concurrent or sequential administration of intravenous immunoglobulin (IVIG) and/or therapeutic plasma exchange. Within the context of our clinical practice, therapeutic plasma exchange constitutes the most frequently employed second-line therapeutic modality. A clinically significant response to therapeutic plasma exchange typically becomes evident following the third or fourth therapeutic session. Potential complications associated with therapeutic plasma exchange include Bleeding complications, hypocalcemia, procedural pain, hypotension, and an elevated risk of infection related to the placement of a central venous catheter.

Hyperacute and fulminant presentations of ADEM may significantly elevate intracranial pressure, necessitating prompt medical intervention. Therapeutic strategies should encompass hyperosmolar therapy to mitigate cerebral edema and the administration of barbiturate medications to attenuate metabolic demands within the central nervous system. In cases of fulminant and refractory ADEM, where standard therapies prove inadequate, immunomodulatory agents such as rituximab and cyclophosphamide may be employed as second-line interventions with varying degrees of clinical efficacy. Early and comprehensive rehabilitation, including physical, occupational, and speech therapies, is pivotal for maximizing functional recovery.[13]

CONCLUSION

This case report serves as a testament to the successful clinical management of a patient afflicted with acute disseminated encephalomyelitis. Prompt recognition of ADEM is paramount in patients presenting with an altered sensorium following a history of viral infection. Rigorous patient monitoring is imperative, with a particular emphasis on the expeditious reporting of any emergent symptoms or adverse drug reactions, particularly those associated with corticosteroid therapy. This proactive approach facilitates timely intervention and optimizes long-term patient outcomes.

CONFLICTS OF INTEREST

The authors declare no conflict of interest.

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