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Case Report

Internal Medicine Section

A Case of Acute Disseminated Encephalomyelitis in Adults: Unravelling the Influenza B and Leptospirosis Co-infection

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ABSTRACT

Acute Disseminated Encephalomyelitis (ADEM) is a neurological disorder characterised by demyelination, where the immune system targets the Central Nervous System (CNS). This condition typically develops rapidly, with neurological symptoms appearing within days to weeks following viral infections or immunisations. Before the onset of neurological manifestations, patients often experience systemic symptoms such as fever, headache, malaise, and myalgias. The transition from the febrile phase of illness to neurological symptoms generally occurs with a latency period of 7 to 14 days. ADEM is commonly referred to as "post-infectious," "para-infectious," "post-exanthematous," or "post-vaccinal" encephalomyelitis. Recognised as a potential cause of permanent neurological disability, ADEM frequently affects individuals early in life, underscoring the significance of understanding this disease entity, particularly in the context of routine immunisation practices. Herein, the authors present the case of a 28-year-old female, who presented with quadriparesis in a drowsy state following a febrile illness. Upon further evaluation, she was diagnosed with a co-infection of Influenza B and leptospirosis, confirmed by positive serological tests. Magnetic Resonance Imaging (MRI) of the brain revealed hyperintensities suggestive of ADEM in multiple areas of the brainstem and thalamus, while Cerebrospinal Fluid (CSF) examination showed an albumin-cytological dissociative picture, further supporting the diagnosis. Treatment comprised a pulse steroid regimen followed by oral steroid tapering. Subsequently, the patient demonstrated clinical improvement over the course of a week, with progressive enhancements observed during follow-up assessments. The present case highlights the importance of prompt recognition and management of ADEM, emphasising the role of corticosteroid therapy in achieving favourable patient outcomes.

Keywords: Immunisation, Infection, Neurological, Quadriparesis, Steroids

CASE REPORT

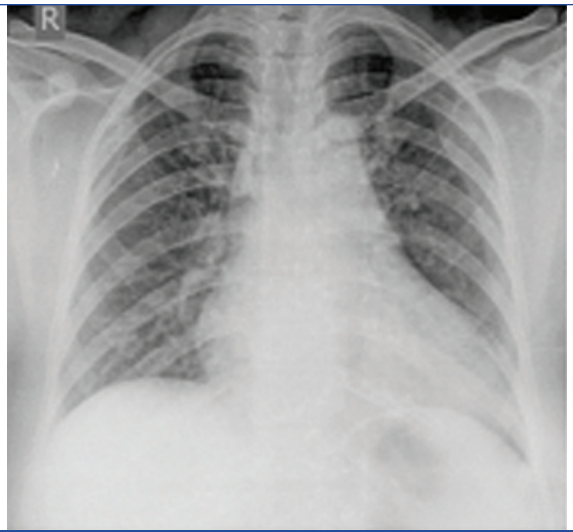
A 28-year-old female presented to the hospital with a history of symptoms including headache, cough, intermittent fever, and weakness persisting for 7 to 10 days. She had a high fever of 101°F about a week prior and sought medical attention at a local clinic, receiving symptomatic treatment before her discharge. Four days later, she developed myalgia and visited another private clinic for symptomatic therapy, again without significant improvement. Despite returning home, she continued to feel weak, lethargic, and unable to mobilise, experiencing heaviness in all four limbs. Consequently, she was brought to the hospital for further evaluation. In addition to the aforementioned complaints, the patient reported double vision and slurring of speech with a nasal twang. However, she maintained the ability to swallow food and liquids.

Upon general examination, the patient exhibited an average build and appeared moderately nourished. She presented with fever, registering a body temperature of 100°F, along with a pulse rate of 117 beats per minute, blood pressure measuring 96/60 mmHg, a respiration rate of 24 cycles per minute, and an oxygen saturation of 96% on room air. Notably, there were no signs of pallor, icterus, cyanosis, clubbing, or pedal oedema.

While assessing the cranial nerves, it was noted that there was difficulty in the outward movement of the right eye, suggesting involvement of the sixth cranial nerve on the right-side. The other cranial nerves demonstrated normal function. Additionally, the patient reported a history of involuntary micturition with increased frequency and low volume.

Muscle tone exhibited an increase in all extremities, with power graded as 3/5 in both upper limbs and 2/5 in both lower limbs. Exaggerated reflexes were noted in all four limbs, and there was evidence of ill-sustained clonus at the ankles bilaterally. Babinski sign was elicited on both sides. The rest of the CNS examination showed normal findings. The respiratory system assessment revealed bilateral crepitations upon auscultation, whereas the examination of other systems yielded normal findings. Based on these clinical observations, potential differential diagnosis for this case included bacterial or viral meningitis, bacterial or viral encephalitis, demyelinating disorders such as ADEM, Guillain-Barré syndrome, and Multiple Sclerosis (MS). However, the provisional diagnosis in this particular instance was more consistent with ADEM.

The Chest X-ray revealed bilateral homogeneous opacities [Table/Fig-1]. A Computed Tomography (CT) scan of the brain was performed, which revealed no obvious abnormality. In order to



[Table/Fig-1]: Chest X-ray postero anterior view showing bilateral homogenous opacities.

obtain CSF, a Lumbar Puncture (LP) was conducted. The CSF routine microscopy results indicated typical findings, except for a raised protein level of 117 mg/dL [Table/Fig-2]. Further investigations showed a mildly elevated Total Leucocyte Count (TLC) and thrombocytopenia, in addition to elevated liver enzymes. The real-time Reverse Transcriptase-Polymerase Chain Reaction (RT-PCR) assay confirmed the presence of Influenza type B virus. Subsequent investigations for other infections yielded a positive result for leptospira Immunoglobulin M (IgM) [Table/Fig-3]. Ultrasonography of Abdomen and Pelvis (USG-A/P) revealed no abnormality.

Variables	Findings
Appearance	Clear, transparent
Deposits	Absent
Proteins (mg/dL)	117
Glucose (mg/dL)	80
RBCs	Absent
Total leucocyte count (/cumm)	20
Polymorphs/neutrophils	0%
Lymphocytes	100%
Macrophages	0%
Pleomorphic cells	0%
Adenosine deaminase (U/L)	2.26

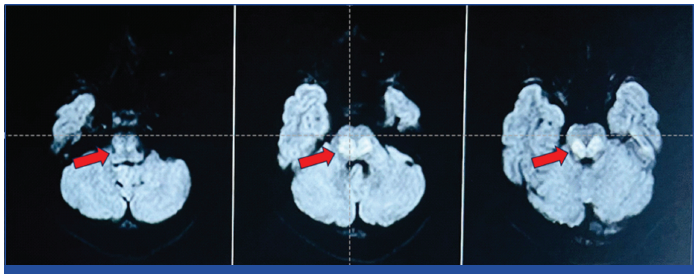
[Table/Fig-2]: Cerebrospinal Fluid (CSF) analysis.

Parameters	Results
Haemoglobin (gm%)	12.8
Total leucocyte count (cells/cumm)	10,500
Platelets (/mm^3)	98,000
Total bilirubin (mg/dL)	1.77
Direct bilirubin (mg/dL)	0.78
Aspartate transaminase (U/L)	133
Alanine transaminase (U/L)	117
Alkaline phosphatase (U/L)	49
Urea (mg/dL)	28
Creatine (mg/dL)	1.17
Serum sodium (mEq/L)	137
Serum potassium (mEq/L)	4.17
C-Reactive Protein (mg/dL)	17
Procalcitonin (ng/mL)	2.7
Antibodies against cytoplasmic components	Weak positive (1:100)
Human Immunodeficiency Virus (HIV)	Non reactive
Hepatitis B surface antigen (HBsAg)	Non reactive
Hepatitis C Virus (HCV)	Non reactive
COVID-RT-PCR	Negative
Influenza-RT-PCR	Influenza type B virus detected
Leptospira IgM	Positive
Dengue IgM/IgG/NS1	Negative
Blood cultures	No growth

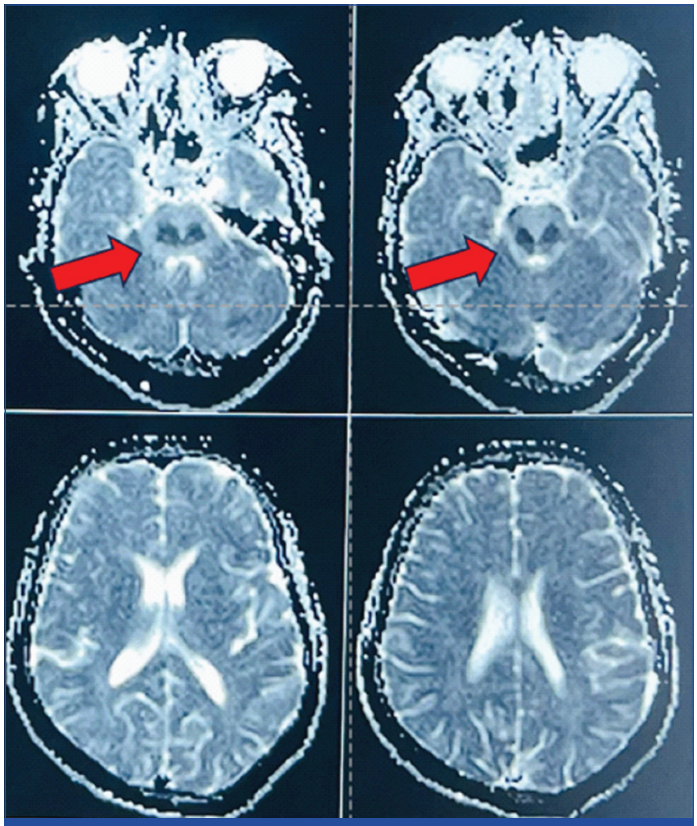
[Table/Fig-3]: Laboratory investigations.

The MRI brain (plain+contrast) revealed Fluid-attenuated Inversion Recovery (FLAIR) hyperintensity in the entire midbrain, pons, and anterior part of the medulla with patchy areas of restricted diffusion. Patchy areas of FLAIR hyperintensity were also noted in both the cerebellar parenchyma and bilateral thalami, not showing restricted diffusion on Diffusion-weighted Imaging (DWI) or blooming on Gradient Echo (GRE) Sequence. All these features are suggestive of ADEM [Table/Fig-4-7].

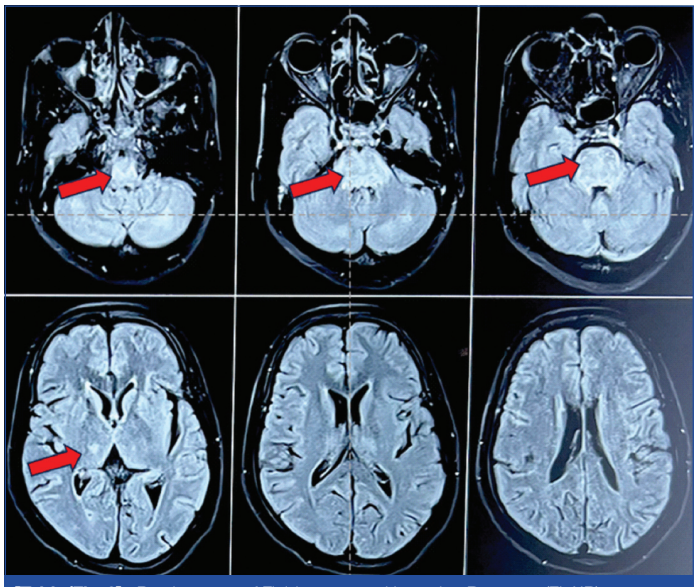
Based on the aforementioned investigations, the patient was diagnosed with ADEM secondary to co-infection with Influenza type B virus and leptospirosis, presenting as acute quadriparesis with right lateral rectus palsy. Treatment commenced with Intravenous administration of Acyclovir 500 mg thrice daily for seven days, Doxycycline 100 mg twice daily for five days along with 1 gm



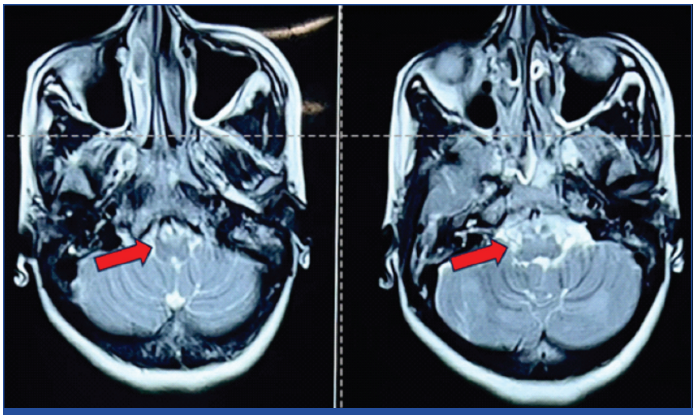
[Table/Fig-4]: Magnetic Resonance Imaging (MRI) Fluid-attenuated Inversion Recovery (FLAIR) sequence - showing hyperintensities noted in the pons, midbrain and anterior part of medulla. (Images from left to right)



[Table/Fig-5]: Magnetic Resonance Imaging (MRI)- Diffusion-weighted Imaging (DWI) sequence-showing patchy areas of restricted diffusion and haemorrhagic areas in pons.



[Table/Fig-6]: Patchy areas of Fluid-attenuated Inversion Recovery (FLAIR) hyperintensity were also noted in both the cerebellar parenchyma and bilateral thalami.



[Table/Fig-7]: T2-weighted hyperintensity was noted in the pons, adjacent portions of the midbrain, medulla oblongata.

Methylprednisolone once daily for five days, followed by a tapering dose of oral steroids. The patient's symptoms had shown notable improvement within a week. On discharge, the patient was able to walk with assistance. During subsequent follow-up, the patient started walking without assistance and resumed her daily activities.

DISCUSSION

The ADEM, also known as post-infectious encephalomyelitis, is characterised by autoimmune-driven demyelination of neurons within the CNS, typically triggered by a preceding infection or immunisation [1]. Approximately, 50% to 80% of cases of ADEM have been attributed to a specific cause of infection or immunisation [2].

The ADEM is diagnosed by assessing the patient's medical history, neurological symptoms, neuroimaging, and CSF. When making a differential diagnosis, MS and acute viral encephalitis are the main possibilities. ADEM and MS have comparable pathophysiologic features; however, clinical symptoms and disease progression differ. ADEM is characterised by a history of infection, fever, systemic symptoms, consciousness changes, neurological dysfunctions, seizures, and movement issues. These symptoms are not seen in MS [3]. Leptospirosis is a common zoonotic disease caused by bacteria of the Leptospira genus [4]. The clinical triad of conjunctival infection, Acute Kidney Injury (AKI), and jaundice termed Weil's syndrome is the most classical presentation of leptospirosis [5]. The clinical course of leptospirosis includes an anicteric phase and a more benign icteric phase [6]. Around 10-15% of cases involve the neurological system, with meningitis, encephalitis, and cerebral arteritis being the most prevalent manifestations. Neuroleptospirosis has an incidence rate of about 0.86%. Aseptic meningitis represents the most frequent form of CNS involvement in neuroleptospirosis [4]. Leptospirosis can be caused by direct invasion of the CNS or an immune-mediated reaction to the pathogen [6]. Neuroleptospirosis' clinical symptoms are mostly caused by capillary endothelial injury and vasculitis.

Leptospirosis primarily affects microvascular endothelial cells, resulting in haemorrhagic vasculitis and microcirculation malfunction, which causes cerebral arteritis. The activation of autoreactive lymphocytes (by a non-specific inflammatory process) that enter the CNS via a brief blood-brain barrier breach may contribute to the development of ADEM [4].

The influenza virus primarily causes encephalopathy and seizures as symptoms of CNS damage. Compared to influenza B, influenza A is more frequently associated with neurological involvement [7]. The reported incidence of Influenza-associated encephalitis complications was 17% [8]. Although children are significantly more frequently afflicted with influenza-associated encephalopathy than adults, there have been two cases reported of influenza-B-associated encephalopathy that exhibited symptoms consistent with encephalitis, including virus infection, normal MRI, and Elecroencephalogram (EEG) findings [7,9].

Neuroimaging is crucial for diagnosing ADEM. ADEM diagnosis is much better with an MRI than a Computed Tomography (CT) scan. Early in the disease, a brain CT scan may appear normal. However, anomalies may appear five to fourteen days after disease onset. These anomalies may present as multifocal white matter subcortical lesions [10]. MRI changes occur sooner, usually when neurological symptoms appear. ADEM MRIs show several substantial lesions in the cerebral hemispheres' subcortical and central white matter, cerebellum, brainstem, and spinal cord [11]. Treatment for ADEM focuses on lowering inflammation in the brain and spinal cord. The initial line of treatment for ADEM is typically intravenous steroids. Multiple infusions followed by oral steroids may be needed to complete the treatment. Plasmapheresis and intravenous immunoglobulin therapy may help save lives in patients who do not respond to steroid treatment [12]. In the present case, the patient presented with an acute onset of weakness of all four limbs, which was rapidly progressive with a preceding history of cough, fever, myalgia, and weakness for about 7 to 10 days. Further investigations confirmed the presence of leptospirosis along with an influenza-B coinfection. Additional intracranial infections were ruled out through examination of CSF; additionally, the CSF showed albuminocytological dissociation, suggesting the occurrence of demyelination. Plain and contrast MRI of the brain revealed FLAIR hyperintensities in the entire midbrain, pons, and the anterior part of the medulla. These findings indicate the presence of an acute phase of demyelination of neurons. All of these clinical and radiological symptoms, together with a proven history of leptospirosis and influenza-B, supported the diagnosis of ADEM. The patient's symptoms improved after a week of receiving five days of methylprednisolone pulse therapy, followed by oral steroids along with an intensive course of antibiotics and antivirals.

CONCLUSION(S)

In conclusion, the authors present an exceptionally rare case of ADEM in which the co-infection of influenza B and leptospirosis led to a serious neurological outcome. Despite the extremely low incidence of this neurological complication following this co-infection, medical practitioners should be aware of its potential development due to its rarity. Prompt diagnosis of the condition, coupled with prompt administration of corticosteroid therapy, is associated with a highly favourable and rapid recovery of the patient. In ADEM, MRI is a valuable tool for identifying specific disease-related abnormalities in the brain.

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