A Rare Presentation of Encephalopathy in a 3-Year-Old Child

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Presentation
A 3-year-old boy with no known significant past medical history apart from mild speech delay presented with a 10-day history of an upper respiratory infection and intermittent low-grade fever followed by irritability, lethargy, and an unsteady gait. He had complained of diffuse body aches. Parents denied any rash, vomiting or diarrhea, seizures, drug ingestion, or head injury. There was no history of recent travel or vaccinations. Immunizations were up-to-date. On admission, vitals were as follows: blood pressure 123/57 mm Hg, pulse 141/min, temperature 37.5°C (oral), respiratory rate 32/min, height 96.5 cm, weight 17.237 kg, body mass index 18.51 kg/m², and SpO₂ 100%. On general examination the child was sleepy, lethargic, barely opening his eyes, and not responding to verbal commands. HEENT: locked jaw with drooling. No neck stiffness. Lungs were clear to auscultation. There was no cardiac murmur. Abdomen was soft, with no apparent tenderness without hepatosplenomegaly. He had no rash. Neurological examination showed pupils were 2 mm and equally reactive to light, no nystagmus, and decreased right-sided naso-labial fold. He withdrew extremities to deep painful stimuli with relative decreased movement on the left side. He had hypertonia of the ankles bilaterally with a few beats of clonus. He was hyperreflexic in the upper and lower extremities and plantar responses were extensor bilaterally.

Diagnosis
Laboratory findings showed a normal blood cell count along with a normal metabolic panel including normal liver function testing. Spinal fluid analysis was unremarkable. Cerebrospinal fluid oligoclonal antibodies and IgG index were normal. Electroencephalogram showed diffuse slowing with no focal abnormality, no epileptic discharges, or seizures. Computed tomography of the head showed opacification of paranasal sinuses and mastoid air cells. Magnetic resonance imaging (MRI) findings are shown in Figures 1 and 2.

Differential Diagnosis
1. Multiple sclerosis
2. Optic neuritis
3. Transverse myelitis
4. Meningitis/encephalitis
5. Neuromyelitis optica

The Condition
Acute disseminated encephalomyelitis (ADEM), also known as “postinfectious,” “parainfectious,” “postexanthematous,” or “postvaccinal” encephalomyelitis, is an immune mediated demyelinating disease of the central nervous system that typically presents as a monophasic disorder associated with multifocal neurologic symptoms and encephalopathy.¹ Pathogenesis of ADEM is incompletely understood. The proposed mechanism is that myelin autoantigens, such as myelin basic protein, proteolipid protein, and myelin oligodendrocyte protein, share antigenic determinants with those of an infecting pathogen.² The immunopathological events leading to ADEM can be divided into 2 major phases: (1) initial T-cell priming and activation and (2) subsequent recruitment and effector phase.³ The estimated incidence of ADEM from different causes has been reported to be between 0.4 and 0.8 per 100,000 of population. ⁴ Clinically, ADEM should be suspected in a child who develops encephalopathy-like symptoms and multifocal neurological signs post 2 weeks.

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of a viral infection or vaccination. Fifty percent to 75% of children present with acute febrile illness 4 weeks prior to the onset of typical neurological symptoms, which appear 4 to 13 days after an infection or vaccination.\textsuperscript{4,6-9} Initial presentation often consists of fever, headache, vomiting, seizures and meningismus.\textsuperscript{10,11} Encephalopathy is the characteristic feature and develops rapidly in association with multifocal neurologic deficits.\textsuperscript{12} Other common neurologic features include long tract (pyramidal tracts) signs, acute hemiparesis, cerebellar ataxia, cranial neuropathies including optic neuritis, and spinal cord dysfunction (transverse myelitis).\textsuperscript{7-12}

**Diagnostic Criteria**

Diagnostic criteria for ADEM in children were proposed by the International Pediatric Multiple Sclerosis Study Group in 2007 and updated in 2012\textsuperscript{13}:

1. **Monophasic ADEM:**
   a. A first polyfocal clinical central nervous system event with presumed demyelinating inflammatory cause
   b. Encephalopathy that cannot be explained by fever is present
   c. MRI typically shows diffuse, poorly demarcated, large, >1 to 2 cm lesions involving predominantly the cerebral white matter; T1 hypointense white matter lesions are rare; deep grey matter lesions (eg, thalamus or basal ganglia) can be present
   d. No new symptoms, signs, or MRI findings after 3 months of the incident ADEM

2. **Recurrent or multiphasic ADEM:**
   a. New event of ADEM 3 months or more after the initial event that can be associated with new or reemergence of prior clinical and MRI findings. Timing in relation to steroids is no longer pertinent.

The diagnosis of ADEM is based on both clinical and radiologic features.\textsuperscript{11} There are no specific biological markers and confirmatory tests. A lumbar puncture
must be performed to rule out acute infectious meningoencephalitis. Complete blood count, cultures, and serologic tests must be performed on blood and cerebrospinal fluid to detect bacterial and viral organisms. Cerebrospinal fluid immunologic analysis may show transient appearance of oligoclonal bands and lymphocytic pleocytosis. The most widely applied diagnostic tool is brain and spine MRI.

Monophasic ADEM
Brain MRI, with FLAIR or T2-weighted images, shows large (>1-2 cm in size) lesions that are multifocal, hyperintense, and located in the supratentorial or infratentorial white matter, grey matter, and especially basal ganglia and thalamus. In rare cases MR images show a large single lesion predominantly affecting white matter. Spinal cord MRI may show confluent intramedullary lesions with variable enhancement.

Multiphasic ADEM
Brain MRI must show new areas of involvement but also demonstrate complete or partial resolution of those lesions associated with the first ADEM event.

Management
Intravenous high-dose steroid treatment, based on empirical evidence (type C recommendation) has been the most widely reported first-line therapy for ADEM. There are multiple case reports of IVIG being used successfully alone or in combination with corticosteroids in both pediatric and adult cases of ADEM, but there have been no studies that have directly compared IVIG with steroids, plasmapheresis, or other immunomodulatory treatments. The use of plasma exchange in ADEM has been reported in only a small number of cases, typically severe cases when steroid treatment has failed.

Prognosis
Most children with ADEM make a full recovery, usually slowly over 4 to 6 weeks. At follow-up, approximately 60% to 90% have minimal or no neurologic deficits.

Conclusion
ADEM should be considered in the differential in children presenting with acute encephalopathy that cannot be explained by an infectious etiology.

Author Contributions
EK: Contributed to conception and design; contributed to acquisition; drafted manuscript; gave final approval; agrees to be accountable for all aspects of work ensuring integrity and accuracy.
DM: Contributed to acquisition; drafted manuscript; gave final approval; agrees to be accountable for all aspects of work ensuring integrity and accuracy.
AK: Contributed to conception and design; contributed to acquisition; critically revised manuscript; gave final approval; agrees to be accountable for all aspects of work ensuring integrity and accuracy.

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