CASE REPORT

A Baby with Acute Encephalopathy, Refractory Hyponatremia, and Hypertension: A Case Report

Gajalakshmi S H[1], Jigna N Bathia[2], Hriday De[3], Deblina Dasgupta[4], Priyankar Pal[5]

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Abstract

Autoimmune encephalitis (AE) is an expanding group of clinical syndromes that can occur at all ages (from <1 year to adult), but more commonly affects young adults and children. It is a rare cause of encephalopathy that has been increasingly recognized over the last decade. Most of these disorders are severe and potentially fatal; however, if recognized in a timely manner and treated with immunotherapy, patients often respond well with good outcomes. Here, we present a 7-month-old baby girl with seronegative AE, presenting with encephalopathy, hypertension, and refractory persistent hyponatremia. Prompt treatment with aggressive immunotherapy improved her neurological symptoms. This case highlights the association of hyponatremia, hypertension, and the importance of timely immunotherapy in AE.

Keywords: Anti-NMDAR encephalitis, Adolescent psychiatry, Autoimmune encephalitis, Case report, Functional neurological disorder, Immunotherapy, Pediatric neuroimmunology.

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Key Learning Points

- Autoimmune encephalitis (AE) is a broad spectrum of diseases which needs further investigation and studies to detect potential antibodies.
- Seronegative AE has more severe neurological impairment and poor outcome compared to seropositive AE.
- Autoimmune encephalitis might be associated with unusual features like electrolyte imbalance (hyponatremia, hypokalemia) and SIADH which is not mentioned in literature especially in pediatrics population.
- FDG-PET imaging aids in early diagnosis of AE especially in seronegative AE and helps in characterizing the type of AE based on metabolic patterns.
- Autoimmune encephalitis is not a monophasic illness. Relapse have been noted even after 5–10 years.
- Aggressive immunotherapy plays a critical role in treatment and to achieve good prognosis. Rituximab is effective in refractory cases.

[1–3]Department of Pediatrics, Institute of Child Health, Kolkata, West Bengal, India

[4]Department of Pediatric Nephrology, Institute of Child Health, Kolkata, West Bengal, India

[5]Department of Pediatric Rheumatology, Institute of Child Health, Kolkata, West Bengal, India

Corresponding Author: Gajalakshmi S H, Department of Pediatrics, Institute of Child Health, Kolkata, West Bengal, India, Phone: +91 8050197776, e-mail: gajalakshmishgaja@gmail.com

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Introduction

Autoimmune encephalitis is an expanding group of clinical syndromes that can occur at all ages (from <1 year to adult), but it more commonly affects young adults and children. It is a rare cause of encephalopathy that has been increasingly recognized over the last decade. Although its exact mechanism remains unclear, current research indicates that autoimmune antibodies target synaptic proteins, triggering brain inflammation.[1] It has a wide clinical spectrum that ranges from typical limbic encephalitis to syndromes with complex neuropsychiatric symptoms such as altered sensorium, loss of memory, cognition, psychosis, seizures, electrolyte imbalance, autonomic dysregulation, or coma.[1–3] Seronegative AE refers to a subgroup of AE where the patient does not have detectable antibodies in cerebrospinal fluid (CSF) or serum. The possible reasons for the absence of antibodies maybe decreasing serum antibodies or the existence of unidentified antibodies which are yet to be discovered or the non-availability of tests to detect the less common serotypes.[4] This makes the diagnosis and treatment more challenging. Early recognition and treatment prevent relapse and reduce long-term neurological sequelae. Management of AE is mainly by using immunosuppressants. First-line therapy includes steroids and intravenous immunoglobulins (IVIG).[5–12] Second-line immunotherapy, such as rituximab or cyclophosphamide, should be considered if the symptoms do not subside with the first-line therapy.[6,12–14]

Case Presentation

A 7-month-old baby girl presented with complaints of generalized tonic-clonic seizures for 90 min. The convulsions were aborted by benzodiazepine at the emergency, and the baby was admitted for further evaluation. After thorough history and physical examination,

it was found that she was a full-term *in vitro* fertilization born baby with no significant birth or past history. The present history started 2 days ago when the parents noticed that the baby was drowsy and had low-grade fever (100–101°F) following vaccination. Examination findings revealed that the vitals were stable. Systemic examination including the central nervous system was normal. There was post-ictal drowsiness and a few crepitations on chest auscultation.

Investigations

Routine blood investigations were sent. The laboratory workup was unremarkable: TLC – 15,900/mm^3, N57L38; C-reactive protein (CRP): 0.57mg/L (normal range ≤1 mg/L), hyponatremia: 113 mmol/L (normal range 135–145). Liver and kidney function tests were within the normal limits. Urine for routine examination and culture sensitivity was unremarkable. Procalcitonin level was 0.05 ng. Blood culture was negative. Infective causes like dengue, malaria, scrub typhus, and enteric fever were ruled out. Lumbar puncture revealed CSF with normal transparency, 0 leukocytes/mL, 57 mg/mL glucose, and 25 mg/L protein (normal findings). Gram stain and culture were negative.

Management

The baby was admitted, stabilized, and started on Levetiracetam and antibiotics. Routine investigations were normal except for hyponatremia and hypertension (99th percentile for that age and sex). The hyponatremia was resistant to repeated 3% NaCl correction. The hypertension (BP: 110/70 ± 10 mm Hg) persisted despite two anti-hypertensives (Amlodipine and Prazosin) at maximum dosage. Magnetic resonance imaging (MRI) of the brain did not reveal any significant findings other than mildly dilated ventricles. Electroencephalography was normal. Cerebrospinal fluid studies, including the AE antibody panel, were normal. Echocardiography, non-contrast CT (NCCT) of the brain, fundus examination, and USG of kidneys as a part of hypertension workup were also normal. Lumbar puncture showed normal CSF. Gram stain and culture were negative. Laboratory workup was unremarkable except for hyponatremia: 113 mmol/L (normal range 135–145). C-reactive protein was 0.57 mg/L (normal range ≤1 mg/L), and no infection was detected. Considering a immune/inflammatory cause, the baby was administered intravenous immunoglobulin and methylprednisolone pulse therapy for 5 days. However, there was no improvement in her clinical condition. Further evaluation of the hyponatremia revealed raised urinary sodium excretion (211 mEq/L, normal range <20 mEq/L), raised urinary osmolality (561 mOsm), low serum osmolality (269 mOsm), along with raised urinary urates (Table 1). With a provisional diagnosis of syndrome of inappropriate ADH secretion (SIADH), fluid restriction and tolvaptan (6 mg/kg/day) was started. The hyponatremia gradually improved over the next few days (Fig. 1).

Due to ongoing encephalopathy, a repeat MRI was performed, revealing only mildly dilated ventricles. The imaging findings, combined with CSF results and the prolonged duration of illness, made acute disseminated encephalomyelitis less likely. As the hypertension persisted and a neuroendocrine or para-neoplastic cause was suspected, Fluorodeoxyglucose positron emission tomography–computed tomography (FDG PET-CT) scan was done, which revealed increased areas of uptake in bilateral mesial temporal cortices, thalami, basal ganglia, and brain stem, with globally reduced metabolism in rest of the brain (Fig. 2). Persistent encephalopathy, normal CSF studies, normal MRI brain, unexplained hypertension (autonomic/central), and diffuse FDG uptake on PET-CT all pointed toward a final diagnosis of seronegative AE with secondary SIADH refractory to first-line immunotherapy.

Table 1: Table of investigations supporting SIADH

Investigation	*Value*
Serum osmolality	269 mOsm (280–295)
Urine osmolality	561 mOsm
S. sodium	125 mEq/L (135–145)
Urinary sodium	211 mEq/L (<20 mEq)

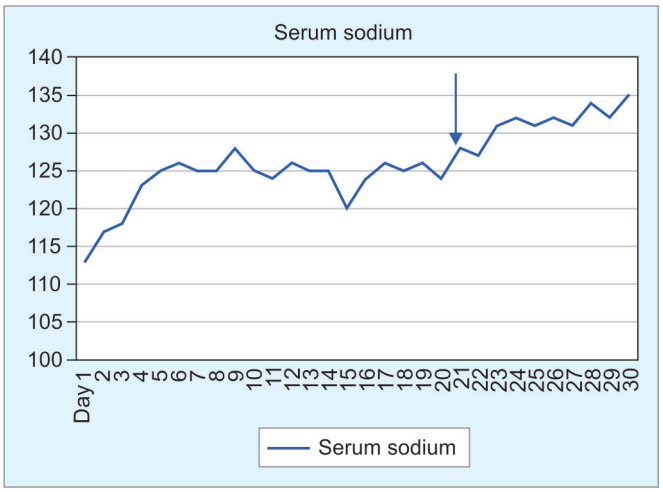

Fig. 1: Trend of sodium. Blue arrow indicates introduction of oral Tolvaptan

Outcome

The baby was started on injection Rituximab (750 mg/m^2) after the final diagnosis. Drowsiness gradually improved over the next 7 days, and she was discharged. A second dose of Rituximab was given after 15 days. On follow-up, tolvaptan and anti-hypertensives have been gradually tapered off and stopped over the next 9 months. She gradually regained her milestones. The child was asymptomatic for the next 15 months and was under regular follow-up.

Later, she developed abnormal movements – myoclonic jerks were noticed by her parents. Repeat imaging did not reveal any significant abnormalities. Considering a relapse of encephalitis, a pulse dose of intravenous methylprednisolone was administered, followed by two doses of Rituximab (750 mg/m^2) was repeated. Currently, the child is asymptomatic and remains under follow-up.

Discussion

Autoimmune encephalitis is a growing group of broad-spectrum clinical syndromes that can affect individuals of all ages, though it is more common in children and young adults. It is a rare but increasingly recognized cause of encephalopathy. While the exact mechanism is still not fully understood, research suggests that autoimmune antibodies target synaptic proteins, leading to brain inflammation.[1–3] In more 50% of cases, antibodies are absent or undetectable with the techniques available currently. This subgroup is categorized as seronegative AE. It requires further study

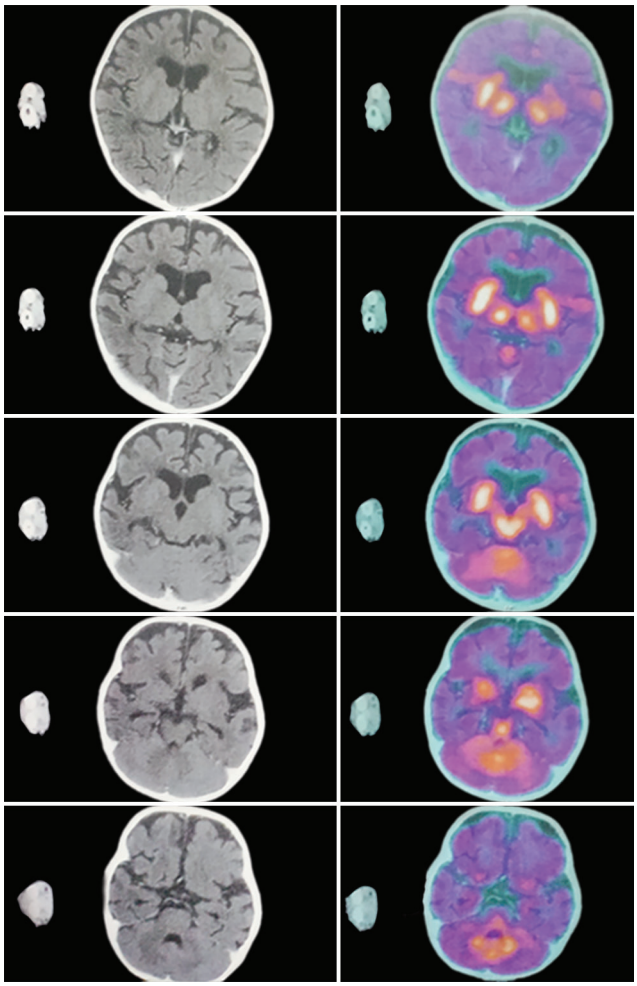

Fig. 2: PET-CT findings. Increased FDG uptake in B/L mesial temporal cortices, thalami, basal ganglia, brainstem with globally reduced metabolism in rest of the brain

and investigation to identify potential antibodies. They have more severe neurological impairment and poor outcome when compared to seropositive AE.[4,15–17] Prompt diagnosis and exclusion of other causes, such as viral encephalitis, are crucial. Evidence indicates that management with earlier initiation of immune-suppressive treatment facilitates better recovery in this potentially fatal condition.[4,6] When AE involves a particular area of the brain, such as the cortical area, focal neurologic deficits such as language dysfunction, motor deficits, and focal seizures occur. Limbic system involvement causes behavioral disturbances, electrolyte imbalance, and cognitive decline. Limbic encephalitis is a subtype where limbic structures of the brain are affected (mesial temporal lobes).[4,7] Diagnosis of AE is based on integration of clinical and test results, including neurological (MRI), electroencephalogram, and immunological (CSF study) results, combined with the exclusion of other diseases (viral encephalitis) that could mimic the observed symptoms. PET-CT imaging has emerged as a crucial tool in the early diagnosis of AE, particularly when MRI results are normal or nonspecific, and studies have shown that PET-CT is more sensitive than MRI in detecting AE, especially in seronegative AE. Basal ganglia hypermetabolism is a characteristic feature in anti-CASPR2 and anti-LGI1 AE, often accompanied by temporal hypermetabolism.[9–11]

This case highlights the association of hyponatremia (secondary SIADH) with AE, which was refractory to repeated sodium correction and responded well to use of tolvaptan.[16,17]

Conclusion

Seronegative AE (antibody negative but possible AE) represents a broader spectrum of disorders that can present with unusual and unexplained symptoms, such as electrolyte imbalance and autonomic dysregulation.[2,3] The disease's association with electrolyte imbalance (hyponatremia, hypokalemia) is seen in leucine-rich glioma-inactivated 1 antibody (LG I1) antibody encephalitis, which is not mentioned in literature, especially in the pediatric population.[5,7,8] FDG-PET imaging aids in early diagnosis, especially when MRI is unremarkable with negative serum and CSF autoantibody profiles, enhancing diagnostic accuracy.[9–11] Aggressive immunotherapy plays a critical role to achieve a good prognosis.[5,6] However, first-line immunotherapy (i.e. corticosteroids) and their efficacy has limited role in seronegative AE. Studies have shown that seronegative AE responds better to second-line immunotherapy (Rituximab and Cyclophosphamide).[5,6,8,12] Rituximab shows an favorable prognosis rate in refractory patients, with particularly greater effectiveness in pediatric population.[13–15]

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