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New Onset Encephalopathy with Toxic Triphasic Waves

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Abstract

New onset encephalopathy can have various causes like stroke, trauma, seizures, infections, demyelination, neoplasms, autoimmune, degenerative, and toxic and metabolic etiologies. Triphasic waves in electroencephalogram (EEG) is usually a clue to an ongoing metabolic process. We report a case of a 69-year-old female with bipolar disorder who presented with altered sensorium for the last 2 days. Her metabolic parameters, imaging, and cerebrospinal fluid findings were normal. Her EEG findings in the clinical setting provided a diagnostic clue to lithium toxicity, even though her serum lithium levels were normal. As her sensorium was progressively worsening, she was given a trial of hemodialysis with which she had significant improvement.

Keywords
- encephalopathy
- lithium toxicity
- triphasic waves

Encephalopathy is an alteration in mental status affecting the patient's cognition or level of arousal. It can have several etiologies that present acutely like stroke, trauma, seizures, or migraine, while infections, demyelination, neoplasms, autoimmune, degenerative, toxic and metabolic etiologies present subacutely.[1] Various metabolic disturbances, illicit-drugs, and several medications can produce toxic and metabolic encephalopathies. Triphasic waves in electroencephalogram (EEG) is a clue to an ongoing metabolic process. Though initially thought to be pathognomonic of hepatic encephalopathy, they can be seen in any metabolic encephalopathy, drug toxicity, and many other conditions. We present a case of new onset encephalopathy where persistence of triphasic waves in EEG was a diagnostic clue to lithium toxicity.

A 69-year-old diabetic, hypertensive female with psychiatric illness for 40 years presented with altered sensorium and decreased word output for 2 days that was preceded by a bout of diarrhea. She had a history of generalized weakness and unsteadiness while walking with swaying for the past 6 months. Her routine medications were escitalopram 10 milligram (mg), quetiapine 100 mg, lorazepam 2 mg, telmisartan 40 mg, and lithium 400 mg daily. She used to handle her medications herself. On examination, patient was afebrile with stable vitals. Her Glasgow Coma Scale (GCS) was E3V2M5; pupils and eye movements were normal. She was moving all limbs equally in response to painful stimulus and had normal deep tendon reflexes with no neck stiffness. Magnetic resonance imaging brain showed small vessel ischemic changes without evidence of any acute insult. She had features of acute kidney injury with a serum creatinine of 2.09 milligram per deciliter (mg/dL), urea of 79 mg/dL, and serum potassium 6.2 millimole per liter (mmol/L). There were no other metabolic abnormalities and creatine phosphokinase was 202 units per liter (U/L). Electrocardiogram

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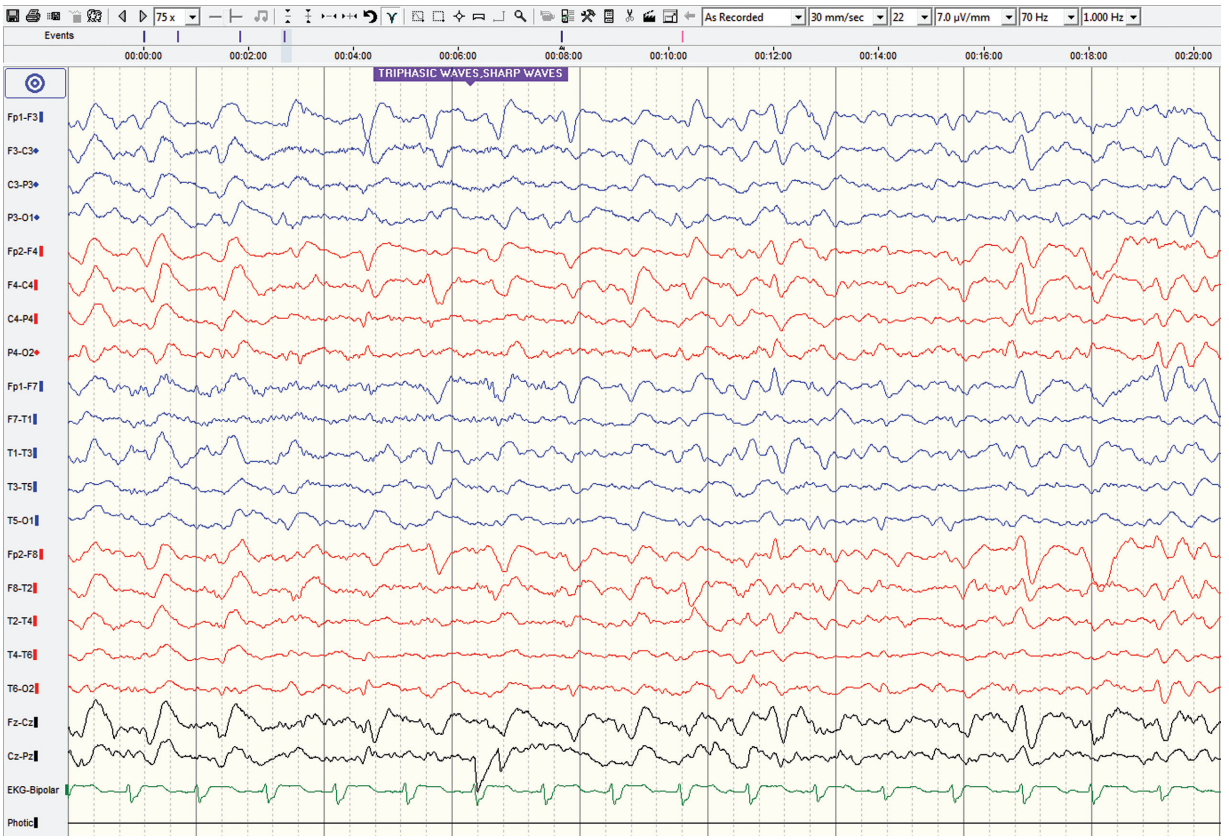

Fig. 1 Electroencephalogram showing diffuse electrophysiological dysfunction with background activity of 3-4 Hz rhythm over posterior head region with frequent triphasic waves and bifrontal sharp waves.

(ECG) showed QT prolongation. EEG revealed diffuse electrophysiological dysfunction with background activity of 3 to 4 Hertz (Hz) rhythm over posterior head region with frequent triphasic waves, bifrontal sharp waves, and persistent low-to-medium amplitude slow waves diffusely (►**Figs. 1** and **2**). In view of the background history of probable ataxia, acute episode being preceded by a bout of diarrhea, history of erratic drug intake, EEG findings, presence of acute kidney, injury and QT prolongation on ECG, lithium toxicity was strongly suspected. Other possibilities considered were acute meningoencephalitis and autoimmune encephalitis. Cerebrospinal fluid (CSF) evaluation showed protein of 61.5mg/dL, no hypoglycorrhachia (sugar 126 mg/dL), and no cells. She was initiated on intravenous acyclovir and steroids empirically while awaiting reports of serum lithium levels and CSF meningoencephalitis and autoimmune encephalitis panels. However, the lithium levels were 0.9 milliequivalents per liter (mEq/L) that were within the normal reference range (0.6–1.2mEq/L), and CSF meningoencephalitis and autoimmune encephalitis panels were negative. Her sensorium progressively worsened to E1V2M2 and EEG changes remained the same despite all measures. Acyclovir and steroids were stopped and a decision to dialyze her was made considering the possibility of lithium toxicity with normal lithium levels as described in literature.[2,3] Her sensorium improved to E3V4 M6 post the first cycle of hemodialysis; hence, she was continued on the same for a total of three cycles till her GCS was E4V5M6 and her EEG abnormalities disappeared (►**Fig. 3**). During the rest of the hospital stay, she developed diabetes insipidus with a urine output of 4.4 L per day, serum osmolality 303 milliosmoles per kilogram (mOsm.kg), and urine osmolality of 187 mOsm/kg. Polyuria decreased with single dose of desmopressin 100 µg. A diagnosis of resolving nephrogenic diabetes insipidus was made attributed to lithium toxicity. Patient was discharged after optimizing medications and was asymptomatic with no focal neurological deficits on follow-up.

Lithium was the first drug to be used in the treatment of bipolar disease and is recommended as first line and maintenance treatment of bipolar disorders due to its neurotrophic effects. However, lithium is a drug with a narrow therapeutic index, ranging from 0.6 to 1.0 mEq/L in serum and the toxic range remains very close to the therapeutic range, from more than 1.5mEq/L. Serum levels of more than 2 mEq/L may be associated with neurological symptoms, including cerebellar dysfunction. Prolonged lithium intoxication can cause permanent brain damage.[4] Features of lithium toxicity are varied, starting from endocrine to renal and central nervous system (CNS) manifestations. Lithium toxicity is characterized by only a mild reduction in glomerular filtration rate, and the absolute risk for renal failure and need for renal replacement therapy remains small.[5] The CNS effects of lithium take several forms, ranging from encephalopathy to SILENT (The syndrome of irreversible lithium-effectuated neurotoxicity) that consists of prolonged neurologic and neuropsychiatric symptoms namely

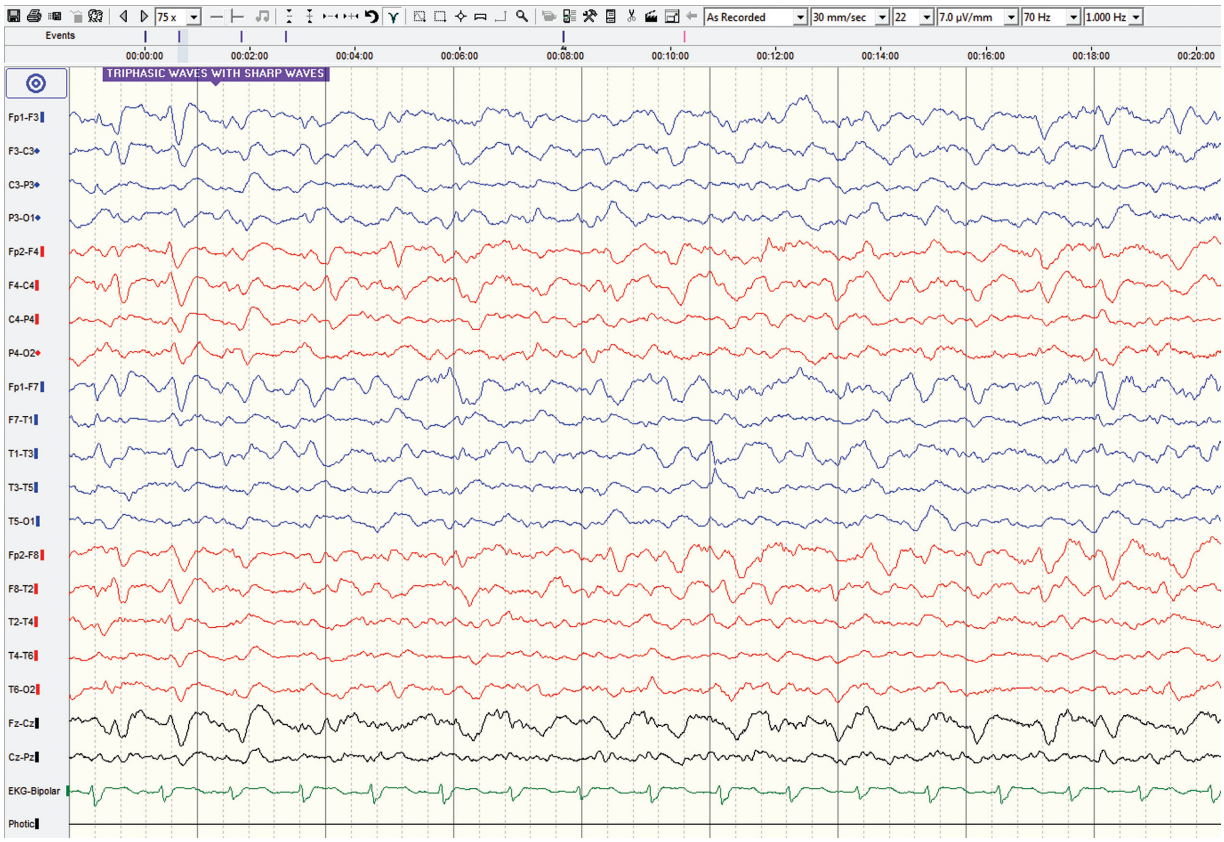

Fig. 2 Electroencephalogram showing prominent triphasic waves and persistent low-to-medium amplitude slow waves diffusely.

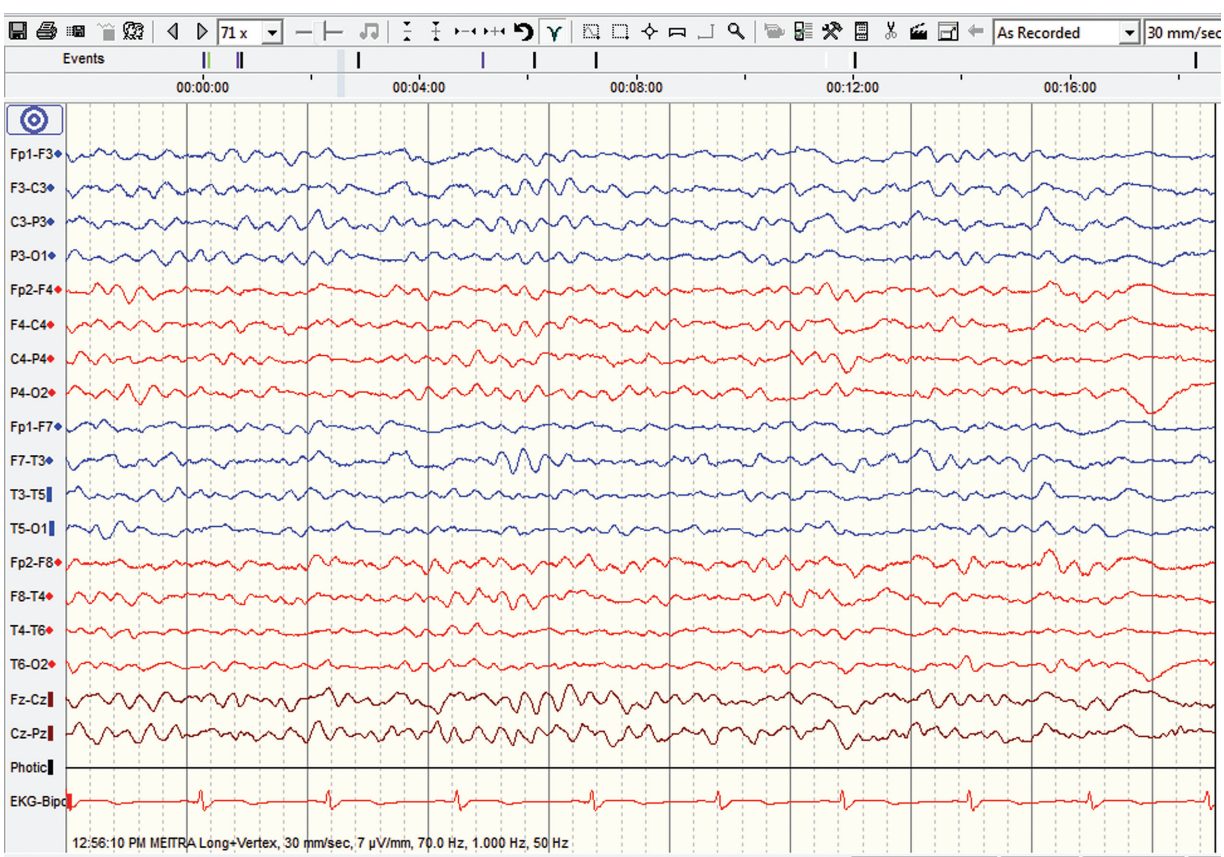

Fig. 3 Electroencephalogram post dialysis showing resolution of triphasic waves and bifrontal sharp waves with improving background of 5-6 Hz over the posterior head region.

cerebellar dysfunction, extrapyramidal symptoms, and brainstem dysfunction.[6] Several EEG changes are described in lithium toxicity, increased amplitude of the alpha rhythms, increased theta and delta activity, triphasic waves, marked bilateral periodic epileptiform discharges and features of nonconvulsive status epilepticus have been reported.[7,8] The main obstacle in front of the clinician while considering lithium toxicity is the fact that there need not always be a direct correlation between the blood levels of lithium and the toxic manifestations.[2] In a study comprising of a retrospective audit of prescriptions for lithium monitoring, 3% of 4,359 prescriptions resulted in toxicity and out of them 60% were in therapeutic range.[3] Rather than plasma lithium levels, red blood cell (RBC) lithium levels correlate better with toxicity and if available an RBC-plasma ratio of lithium would have more utility.[9,10]

EEG can be a valuable tool for the diagnosis, prognostication, therapeutic decision making, and assessment of clinical response to treatment of CNS toxicity due to lithium. From the diagnostic point of view, EEG findings can be a marker of toxicity even with normal or modestly elevated serum lithium levels. When unequivocal findings of toxicity are evident that are not accounted by other metabolic, septic, or toxic etiologies, and if the patient does not improve with conservative management, it is justifiable to proceed with next line of treatment with hemodialysis. A clinical and electrographic improvement following the latter would reiterate the diagnosis.

Our case is unique in that it highlights the role of EEG as a diagnostic aid when the clinician is faced with the difficulty of a normal lithium level in a scenario of high index of clinical suspicion of lithium toxicity.

Conflict of Interest
None declared.

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