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Case Report

Possible levetiracetam induced encephalopathy presenting as electrical status epilepticus: An unknown occurrence

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ABSTRACT

Levetiracetam is a novel, broad spectrum anti-epileptic drug with proven efficacy in generalized as well as focal onset seizures. It has renal elimination with no hepatic metabolism. Levetiracetam induced encephalopathy is rarely reported in literature. Triphasic waves in the electroencephalogram are seen in toxic-metabolic encephalopathies of various aetiology like hepatic encephalopathy, uraemia. We report a patient who was on levetiracetam for acute symptomatic seizures and developed encephalopathy with electroencephalogram showing generalised triphasic waves. These triphasic waves disappeared with intravenous lorazepam but without clinical improvement in sensorium. The electroencephalographic abnormality appeared as electrical status epilepticus which got normalised on discontinuation of levetiracetam. This is the first report of levetiracetam induced encephalopathy presenting as electrical status epilepticus and also depicts electroencephalographic correlate of levetiracetam induced encephalopathy.

1. Introduction

Levetiracetam (LEV) is a novel anti-epileptic drug having a broad spectrum anti-seizure activity in both generalized as well as focal onset seizures. It is a relatively well-tolerated anti-epileptic drug (AED) in both adults and children. It is a new AED with renal elimination and no hepatic metabolism.[1] The most common adverse drug reaction (ADR) have been headache, somnolence, asthenia, drowsiness, behavioural disturbance, worsening of psychiatric symptoms and rarely paradoxical worsening of seizures.[2] The behavioural and psychiatric side-effects with LEV include hostility, irritability, nervousness, anxiety and depression.[3] Encephalopathy occurring following LEV administration is a rare occurrence. We report a patient who presented with acute meningoencephalitis and received LEV for solitary episode of seizure and developed encephalopathy after 4 days.

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Electroencephalography (EEG) was suggestive of electrical status epilepticus that got normalised on discontinuation of LEV.

2. Case report

A 46 year old lady presented to our hospital with the symptoms of fever associated with headache of 3 days duration, with one episode of generalised tonic clonic seizures (GTCS). Headache was diffuse, holocranial associated with vomiting. No visual disturbances, bulbar symptoms or limb weakness. No other comorbidities. On neurological examination, she was conscious but disoriented and used to talk irrelevantly. There was nuchal rigidity. Cranial nerves and motor examination was normal. No other localising or lateralising deficits. Complete haemogram revealed neutrophilic leucocytosis. Renal and hepatic functions were normal. Magnetic Resonance imaging (MRI) brain with contrast images did not show any parenchymal lesion or meningeal enhancement. Cerebrospinal fluid (CSF) analysis showed clear CSF, raised protein with normal glucose level and lymphocytic pleocytosis (protein-62 mg/dl; glucose 48 mg/dl; cells-38; lymphocytes-70%, neutrophils-30%). Electroencephalogram (EEG) on day 2 after admission showed mild diffuse slowing of background rhythm with no epileptiform discharges. She was diagnosed as acute meningoencephalitis probably of viral aetiology and was started on intravenous antibiotics (ceftriaxone), acyclovir and levetiracetam (loading dose 20 mg/kg followed by 500 mg 8th hourly). She had improvement in her sensorium as she became conscious, oriented and obeying to commands within 2 days of admission. CSF herpes simplex virus (HSV) polymerase chain reaction (PCR) was negative and hence acyclovir was stopped after 3 days.

There was decrease in her mental status on day 4 after admission as she became stuporous, not responding to verbal commands and opening eyes briefly to painful stimulus. There was no recurrence of convulsive seizures. Repeat serum electrolytes, calcium, renal and hepatic function including serum ammonia were within normal limits. Computed tomography (CT) of brain did not reveal parenchymal lesion. Repeat CSF showed decrease in cell counts (3/cumm). A possibility of non-convulsive status epilepticus was considered. EEG on day 4 after admission showed diffuse slowing of background rhythm with generalised, triphasic waves (Fig. 1). These triphasic waves disappeared on intravenous administration of lorazepam (4 mg) (Fig. 2). But there was no significant improvement in mental status. A possible drug induced encephalopathy causing non-convulsive status epilepticus was considered in view of non improvement in mental status despite disappearance of triphasic waves with lorazepam. LEV and ceftriaxone are known to cause non-convulsive status epilepticus with EEG showing triphasic waves. LEV was stopped first and substituted with clobazam. Ceftriaxone was continued. Within two days, there was gradual improvement in her mental status as she became conscious, oriented and started feeding herself. Repeat EEG showed normalisation of background rhythm with disappearance of triphasic waves

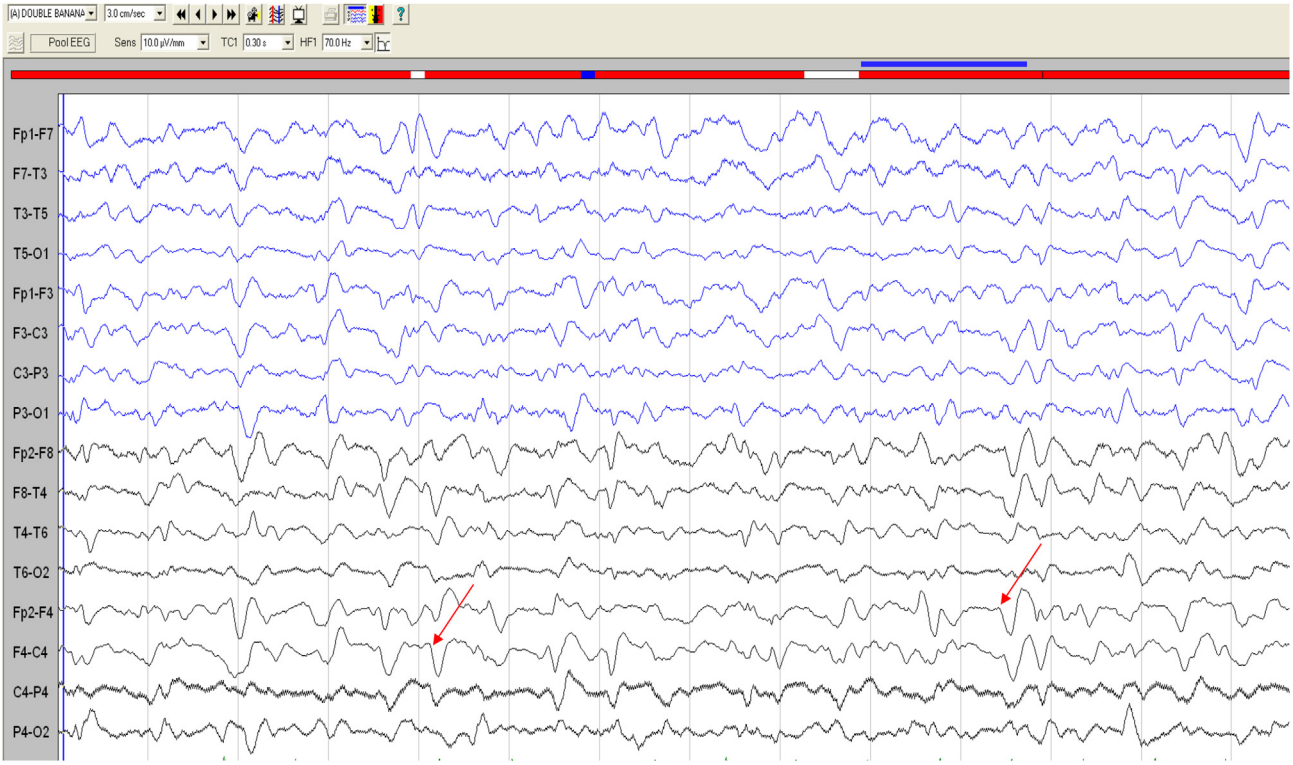

Fig. 1 – Electroencephalogram (EEG) (bipolar longitudinal montage, sensitivity 7.5 μV/mm, low frequency filter 1 Hz, high frequency filter 70 Hz, notch 50 Hz, speed 30 mm/s). Diffuse slowing (frequency 4–5 Hz) of background rhythm with generalised triphasic waves (red arrow).