CASE REPORT

Refractory status epilepticus complicated by drug-induced involuntary movements

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SUMMARY

New onset refractory status epilepticus (NORSE) is a neurological emergency and difficult to treat condition. We report a case of involuntary movements resulting from thiopentone sodium infusion during the management of refractory status epilepticus. A young woman was admitted with fever and NORSE in the neurology intensive care unit. In addition to supportive measures, she was treated with intravenous lorazepam, phenytoin sodium, sodium valproate, midazolam and thiopentone sodium. While on thiopentone sodium, she developed involuntary twitches involving her upper limbs and face with EEG showing no evidence of ongoing status epilepticus. Because of the temporal relationship with thiopentone infusion, we tapered the dose of thiopentone sodium, which resulted in the disappearance of the movements. The patient recovered well with no recurrence of the seizures during the hospital stay.

BACKGROUND

Identifying movement disorder in a patient being treated for refractory status epilepticus is challenging. It can occur due to primary pathology or secondary to the antiepileptic drugs.^{1–3} Identification becomes important as it may be mistaken for ongoing seizure activity and may be treated with increasing dose of antiepileptic drugs or addition of a new antiepileptic drug which may be deleterious and life threatening for the patient. We present the case of a woman who developed intermittent involuntary twitches during the treatment of status epilepticus. It disappeared once the culprit drug was withdrawn.

CASE PRESENTATION

A 24-year-old woman was brought to the emergency department in an unconscious state following frequent generalised tonic-clonic seizures of 3 h duration. She had headache and high-grade fever for 2 days prior to the onset of seizures. She had no seizures or major neurological illnesses in the past. Examination revealed that she was febrile and comatose. Her blood pressure and respiration were normal and there was no neck stiffness. There was no jaundice, petechial haemorrhages or splenomegaly.

INVESTIGATIONS

Haematological investigations like haemoglobin, leucocyte counts, erythrocyte sedimentation rate and peripheral blood smear including examination for malarial parasites were normal. Antigen test for malaria was negative. She had normal liver and renal

function tests. Her cerebrospinal fluid (CSF) examination revealed no cells on microscopy, sugar of 45 mg/dL (blood sugar 120 mg/dL) and protein 45 mg/dL. Herpes simplex virus (HSV) PCR and Japanese encephalitis serology were negative in CSF. Microscopy, antigen test and culture for *Cryptococcus*, microscopy and culture for *Mycobacterium* were also negative in CSF. Brain MRI revealed right external capsule T2 and fluid-attenuated inversion recovery hyper intensity with diffusion restriction. Medial temporal lobes were normal. There was no meningeal enhancement or basal exudates.

DIFFERENTIAL DIAGNOSIS

- *Subtle status epilepticus*: Patients with subtle status epilepticus remain unconscious with subtle jerky movements of the limbs/fingers/eyes. This condition follows an overt status epilepticus. EEG will help to diagnose this condition. Epileptiform discharges will be evident in EEG.⁴
- *Movement disorder due to encephalitic illness*: West Nile encephalitis, N-methyl-D-aspartate (NMDA) receptor-related encephalitis, etc can result in chorea and myoclonus.^{2,5,6} These movement disorders are unlikely to respond to change in medications.
- *Myoclonus secondary to antiepileptic drugs*: Antiepileptic drugs such as phenytoin can cause myoclonus.³ Temporal relationship with the drugs will help in diagnosis.

TREATMENT

Intravenous cannula was inserted and blood was sent for estimating the sugar and electrolytes which turned out to be normal. She was admitted in neurology intensive care unit (ICU) with a provisional diagnosis of encephalitis with status epilepticus. She was promptly given intravenous lorazepam (4 mg) followed by 1000 mg phenytoin sodium with no respite in seizures. Intravenous acyclovir and ceftriaxone were started pending the results of CSF analysis including HSV PCR and MRI of the brain.

Complex partial status epilepticus persisted even after adding intravenous sodium valproate and midazolam. EEG revealed intermittent rhythmic activity arising from the right temporal leads (figures 1 and 2). She was considered to be suffering from Super Refractory Status Epilepticus.⁷ She was intubated and put on intravenous thiopentone 100 mg bolus followed by 100 mg/h infusion. The dose of the thiopentone was titrated to attain cessation in the electrographic seizures. The seizure control was attained at a dose of 2 mg/kg/h of

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Figure 1 Electrographic seizure onset from the right temporal leads.

thiopentone. Continuous EEG monitoring during thiopentone infusion showed no epileptiform activity. Thiopentone tapering was tried after 48 h of seizure-free period, which resulted in breakthrough seizures. Thiopentone sodium infusion was reinstituted at the rate which resulted in seizure control previously. Infusion had to be continued for one more week. While on thiopentone infusion, she developed arrhythmic, asynchronous jerky movements involving bilateral forearms, hands and fingers and, occasionally, over face ([video 1](#)) These movements were intermittent and got aggravated whenever she tried to move her upper limbs. Initially, they were thought to be seizure activity. However, there was no epileptiform discharges in the EEG corresponding to these involuntary movements. The possibility of involuntary movements as part of the primary disease or as an adverse event secondary to thiopentone infusion was considered.

OUTCOME AND FOLLOW-UP

Once thiopentone infusion was slowly tapered the involuntary movements disappeared within 2 days. There was no recurrence of seizures. Her sensorium gradually improved. She made a good recovery and was discharged from the hospital after 2 months. At the time of the discharge, she was on more than

three antiepileptic drugs. Three months after discharge, she has started to look after her baby and cook but with intermittent seizures.

DISCUSSION

We report a case of super refractory status epilepticus complicated by movement disorder during the treatment.⁷ To the best of our knowledge, this is the first case report of super refractory status epilepticus complicated by involuntary twitches secondary to drug. Our patient developed frequent involuntary twitches when she was on thiopentone infusion, which disappeared completely after infusion was tapered and stopped. There are no previous reports of movement disorder while the patient is being treated with thiopentone sodium for refractory status epilepticus. Dystonia and tremor have been reported as a complication of anaesthetic induction with thiopentone, and tremor with propofol.⁸ Propofol has been incriminated as a cause of myoclonus.⁹ It is also a known agent causing various types of seizure-like phenomenon during its induction, maintenance and delayed phase. Movement disorder can be produced by phenytoin administered to control status epilepticus.³ Our patient was also receiving phenytoin sodium and was considered as the possible cause for twitches. However, disappearance of movements

Figure 2 Progression of the seizure to become secondary generalised.

Video 1 Video of the patient showing intermittent twitching movements.

after withdrawal of thiopentone sodium without changing the dose of phenytoin ruled out this possibility. Movement disorder such as chorea has also been reported in children recovering from status epilepticus.¹⁰ Diseases like encephalitis associated NMDA receptor antibodies can cause movement disorder and seizures.¹

A patient with status epilepticus not responding to first-line and second-line anticonvulsant therapy is considered to be in refractory status epilepticus and it is a life-threatening condition. De novo refractory status epilepticus may develop in a person with no previous history of epilepsy. Wilder-Smith *et al*¹¹ reported the clinical syndrome of new onset refractory status epilepticus (NORSE) in a series of seven patients characterised by female gender, young age, previous good health, antecedent febrile illness, CSF pleocytosis, very longlasting status epilepticus, extensive negative workup and catastrophic outcome. Shorvon and Ferlisi⁷ introduced the term 'Super refractory status epilepticus' for status epilepticus that has continued or recurred despite 24 h of general anaesthesia. NORSE forms a

subset of super refractory status epilepticus. Aetiology remains obscure in many cases of NORSE despite exhaustive workup. De novo refractory status epilepticus has been reported in cases of encephalitis and conditions such as Alper's syndrome.¹² It is believed that aetiology of NORSE is heterogeneous with a proportion of it being non-infectious.¹¹ In our patient also, the aetiology remained elusive despite extensive search.

It is important to identify and differentiate subtle movement disorder from seizures because this will prevent patient being exposed to higher dosages of antiepileptic drugs or additional drugs with inherent serious side effects and unnecessary ICU stay. Continuous EEG monitoring will help in the diagnosis, as in our case.

Contributors VW and PPN were involved in conception and design of the manuscript, analysis and interpretation of the data, drafting the article or revising it critically for important intellectual content and approved the final version to be published. SKN was involved in analysis and interpretation of the data, revising the article critically for important intellectual content and approved the final version to be published. AM was involved in acquisition of the data, analysis and interpretation of the data, drafting the manuscript and approved the final version to be published.

Competing interests None.

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Learning points

- ▶ Movement disorder resembling epileptiform activity may arise rarely during the course of status epilepticus.
- ▶ These movements can easily be confused with epileptic activity leading to antiepileptic drug escalation which can be detrimental for the patient.
- ▶ This seizure-like phenomenon may be due to anaesthetic agents, antiepileptic medications or as a direct result of the underlying pathology.
- ▶ EEG is helpful to look for the electrical correlate of the motor activity, and hence avoiding unnecessary escalation of antiepileptic drugs.

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