



Case Report

Myoclonic status epilepticus in six patients without epilepsy[☆]

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ABSTRACT

Myoclonic status epilepticus (MSE) is defined as prolonged period of myoclonic jerks that are correlated with epileptiform discharges on EEG. We here describe clinical features and video-EEG records of six adult patients with MSE who did not have a prior diagnosis of epilepsy. In four out of six patients, MSE was precipitated by drugs. Two out of four patients had chronic renal disease and received beta lactam group antibiotics. Two other patients, who described chronic pain, developed MSE while taking pregabalin. One patient who had dementia and family history of juvenile myoclonic epilepsy (JME) developed MSE one month after quetiapine was introduced. Another patient, who had a recent ischemic stroke, developed MSE due to an unknown reason. In these last two patients, an immediate triggering factor was not evident. Myoclonic status epilepticus ceased in five out of six patients after withdrawal of the drugs and/or intravenous antiepileptic treatment. Myoclonic status epilepticus is a rare event in patients without epilepsy. A correct diagnosis and prompt drug discontinuation may reverse this severe and life-threatening condition.

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1. Introduction

Myoclonic status epilepticus is defined as a condition in which generalized myoclonic jerks are repeated continuously or occur in clusters lasting for a sufficiently long period, usually > 30 min [1]. Myoclonic status epilepticus has been described in generalized epilepsy syndromes, neurodegenerative diseases, toxic-metabolic states, and following anoxic brain injury [2,3]. It is most often seen in patients with insufficiently controlled juvenile myoclonic epilepsy (JME), Dravet syndrome, and in nonprogressive myoclonic epilepsy in infancy, particularly Angelman syndrome [3,4]. In patients with no history of epilepsy, MSE was rarely reported as single case reports, which were mostly drug related [5–7].

We here describe clinical features and video-EEG records, of 6 adult patients with MSE who did not have a prior diagnosis of epilepsy. They were followed up and treated at the Department of Neurology, Ege University Faculty of Medicine, between 2009 and 2011.

2. Case reports

2.1. Patient 1

An 84-year-old man was admitted with hand tremor and jerking movements lasting for 20 days. Past medical history included mild

dementia and type-2 diabetes mellitus. One month earlier, quetiapine 75 mg/day was initiated for delusions and sleep problems. On admission, he was cooperative and exhibited continuous irregular myoclonic jerks mostly of the trunk and upper extremities. His brain magnetic resonance imaging (MRI) scans showed cerebral atrophy. Serum chemistry and blood count were within normal limits. The video-EEG (V-EEG) revealed a well-organized background activity and very frequent bursts of rapid generalized poly-spikes lasting 1–3 s which ceased after intravenous (i.v.) diazepam (up to 10 mg) (Figs. 1A–B). Treatment with levetiracetam 1000 mg/day was introduced and quetiapine was discontinued. A second EEG after six days revealed a nearly normal recording without evidence of epileptiform discharges. Interestingly, a few months later, his 25-year-old grandson was diagnosed with JME.

2.2. Patient 2

A 78-year-old man presented with irregular generalized clonic-twitching movements for more than one week. He had a history of atrial fibrillation and venous insufficiency. His brain MRI scan revealed cerebral atrophy, multifocal chronic ischemic lesions, and subacute ischemic infarct on the left frontoparietal area. Laboratory test results were within normal limits. The V-EEG showed a normal background activity with high-amplitude, 5- to 15-Hz rapid bursts of generalized poly-spikes synchronous with the myoclonia which normalized rapidly after administration of i.v. diazepam (up to 10 mg). The patient remained seizure free and did not report any myoclonia for a follow-up of 1 year under the treatment with levetiracetam 1500 mg/day (see Video sequence 1).

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2.3. Patient 3

A 52-year-old man was hospitalized for gastric variceal bleeding and treated with sclerotherapy. He had a history of renal transplantation 9 years earlier and was receiving hemodialysis for chronic renal disease. Postoperatively, i.v. ceftriaxone and metronidazole were added to his treatment for infection prophylaxis. Three days later, he developed confusion and disorientation. The next day, continuous high-amplitude jerking of the trunk and the extremities appeared which was followed by series of generalized tonic-clonic seizures without full recovery of consciousness in between. His laboratory tests were normal except for an increase in serum creatinine and urea levels (BUN 120 mg/dl, creatinine 6.3 mg/dl). The brain MRI scan was unremarkable. Antibiotic therapy was discontinued. Intravenous diazepam infusion (up to 20 mg) did not cause any clinical improvement. Subsequently, i.v. valproic acid (2000 mg/24 h) was administered. A V-EEG, which was performed 24 h later, showed slowing of background rhythm and high-voltage generalized spike-and-wave discharges (GSWD) which were associated with generalized myoclonia. During intermittent photic stimulation (IPS), violent myoclonic jerks of the eyelids, facial muscles, and the trunk worsened (see Video sequence 2). Unfortunately, after a few days, the patient died due to bleeding complications.

2.4. Patient 4

A 56-year-old woman with a diagnosis of multiple myeloma was hospitalized for bone marrow transplantation (BMT). She developed continuous asynchronous myoclonic jerks mainly of the arms and facial muscles just one day after melphalan hydrochloride (200 mg/m²) chemotherapeutic infusion. She was treated with pregabalin 300 mg/day for chronic pain. Her MRI scans revealed myelomatous infiltration of the skull and durameter. Laboratory test results were unremarkable. The V-EEG consisted of frequent, 5- to 10-Hz, high-amplitude, generalized spikes which lasted 1–3 s and which were suppressed rapidly after diazepam infusion. Pregabalin was discontinued and levetiracetam 750 mg/day was initiated. The patient did not report myoclonia thereafter, but one month later, she died due to BMT complications.

2.5. Patient 5

This 73-year-old woman was admitted to our neurology outpatient clinic with left hemiparesis which occurred due to ischemic stroke 6 months earlier. She had severe burning pain on the side of the body affected by the stroke. She had a history of dementia. Tramadol 50 mg/day and pregabalin 150 mg/day were initiated to relieve central neuropathic pain. Three days later, she exhibited continuous irregular generalized myoclonic jerks. Electroencephalography results showed mild slowing of background rhythm and serial bursts of rapid generalized spikes lasting 1–2 s. After discontinuation of pregabalin, the clinical picture normalized rapidly.

2.6. Patient 6

This 53-year-old man was hospitalized for macroscopic hematuria and treated with transurethral resection (TUR) of the bladder. He had been receiving hemodialysis for chronic renal disease three times a week for 6 years. Postoperatively, since he had fever and hypotension, i.v. meropenem 1000 mg/day was added to his treatment. Five days later, he developed confusion and hallucinations which were followed by generalized myoclonia of the trunk and extremities. His laboratory tests results were normal except for an increase in serum creatinine and urea levels (BUN 60 mg/dl, creatinine 4.61 mg/dl). His brain CT was unremarkable. Antibiotic therapy was discontinued. He did not respond to i.v. diazepam and i.v. valproic acid infusions (2000 mg/24 h).

A V-EEG was performed which showed slowing of background rhythm and GSPW discharges. The myoclonic jerks worsened during intermittent photic stimulation. His myoclonia was diminished after i.v. levetiracetam (1500 mg/day). One week later, he was seizure free and discharged from the hospital. Then, he was diagnosed with bladder cancer. Unfortunately, 2 months later, he died after a cystectomy due to surgery complications.

The clinical and EEG features of the cases are summarized in Table 1.

3. Discussion

Myoclonic status epilepticus is usually reported in patients with epilepsy [4,8]. There are also case reports suggesting that it may be associated with toxic-metabolic brain diseases or induced by drugs in patients without epilepsy [5–7].

None of our patients had a prior diagnosis of epilepsy. Two patients developed MSE while taking pregabalin. In both, withdrawal of the drug led to gradual resolution of the myoclonus. Pregabalin, which is commonly used in chronic pain syndromes, can induce myoclonic jerks in patients with epilepsy and chronic renal failure [5,9]. Pregabalin can also induce generalized and myoclonic SE in patients without epilepsy; however, the mechanism and frequency of this potential adverse effect remain unclear [5]. Two patients had chronic renal disease and received carbapenem and cephalosporin-type antibiotics which can induce a neurotoxic syndrome with encephalopathy and non-rhythmic, stimulus-sensitive myoclonus, especially in patients with renal dysfunction [10,11]. The main mechanism of neurotoxicity appears to involve GABA-A receptor inhibition, although other mechanisms may be possible [11]. The risk of CNS toxicity, especially in seizures, can be increased in renal failure. Patient 1, who had dementia and family history of JME, developed MSE one month after quetiapine was introduced. There are few reports of myoclonus as an adverse effect of higher doses of quetiapine, which interacts with broad range of neurotransmitter receptors, including serotonergic and GABAergic systems [12]; however, we are not sure if this drug was the actual precipitating factor for MSE.

Normal or moderately impaired consciousness and generalized myoclonia were common presentations of our patients. In all patients, myoclonic jerks were generalized, but predominantly affected the upper extremities and showed some asymmetry. In four out of six patients, myoclonias were stimulus sensitive and aggravated with action. Interestingly, in two patients with uremia, myoclonias were increased during IPS. In other patients, this finding was not observed. Photomyoclonic responses and sensitivity to photic stimulation have been noted in uremic patients or renal failure [13]. However, it is rarely reported in the English literature.

Semiology and classification of MSE can be variable. According to Gastaut's classification, pure MSE was observed in patients with epilepsy. Symptomatic MSE occurs as a result of infectious, inflammatory, neurodegenerative, toxic-metabolic, or anoxic brain disease [14]. However, according to Treiman, symptomatic MSE should be considered a subtle presentation of generalized convulsive status, and the term MSE should be used only for pure myoclonic status [15]. Our patients are considered as having symptomatic MSE according to Gastaut's classification.

Myoclonic status epilepticus in patients without epilepsy is a rare event and mostly related with drugs. Cognitive impairment, old age, family history of epilepsy, and decreased creatinine clearance may predispose to this condition. Precipitating drugs such as pregabalin, quetiapine, carbapenem, and cephalosporin-type antibiotics should be avoided in these patients. A correct diagnosis and prompt drug discontinuation may reverse this severe and life-threatening condition.

Supplementary data related to this article can be found online at <http://dx.doi.org/10.1016/j.ebcr.2012.10.003>.

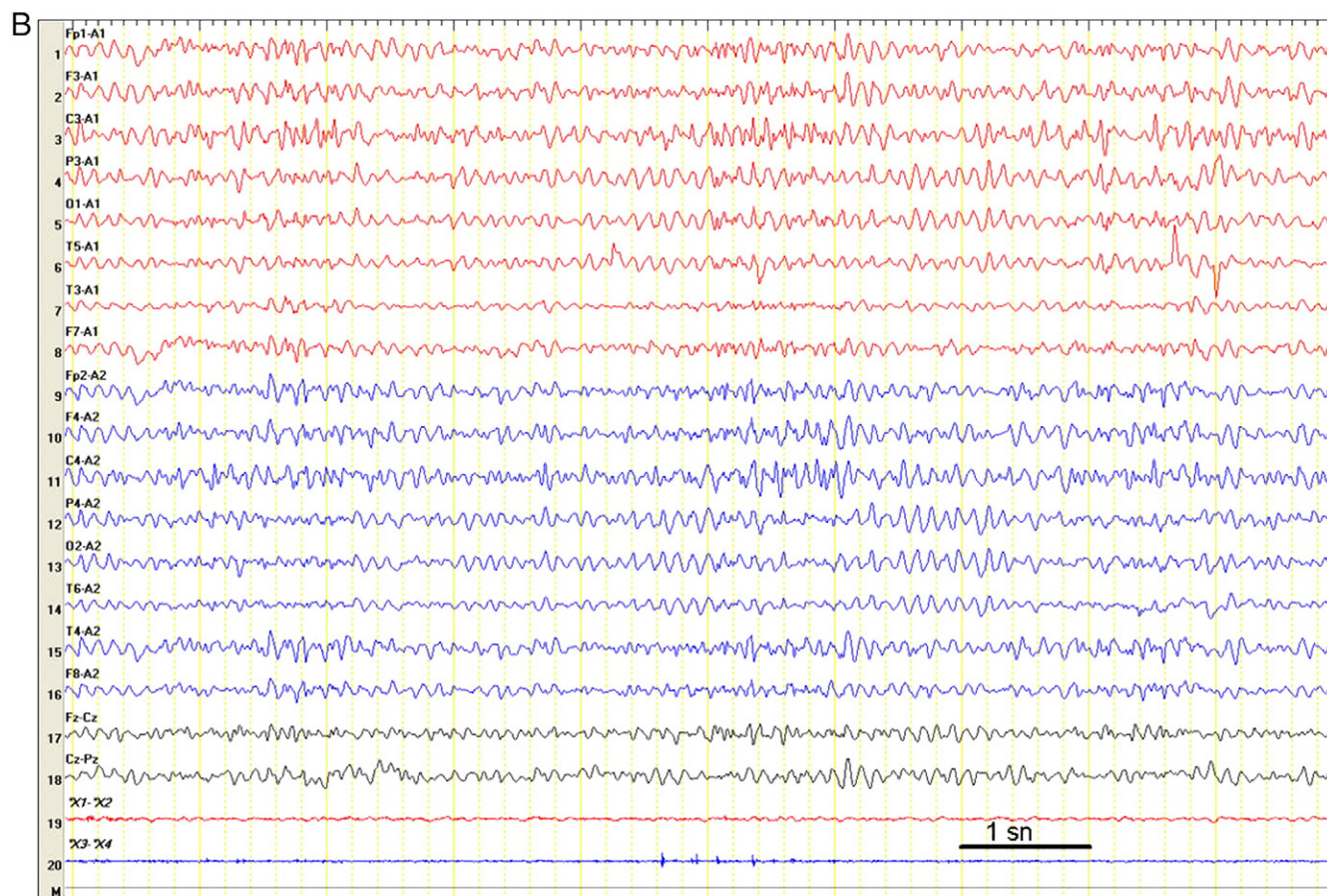
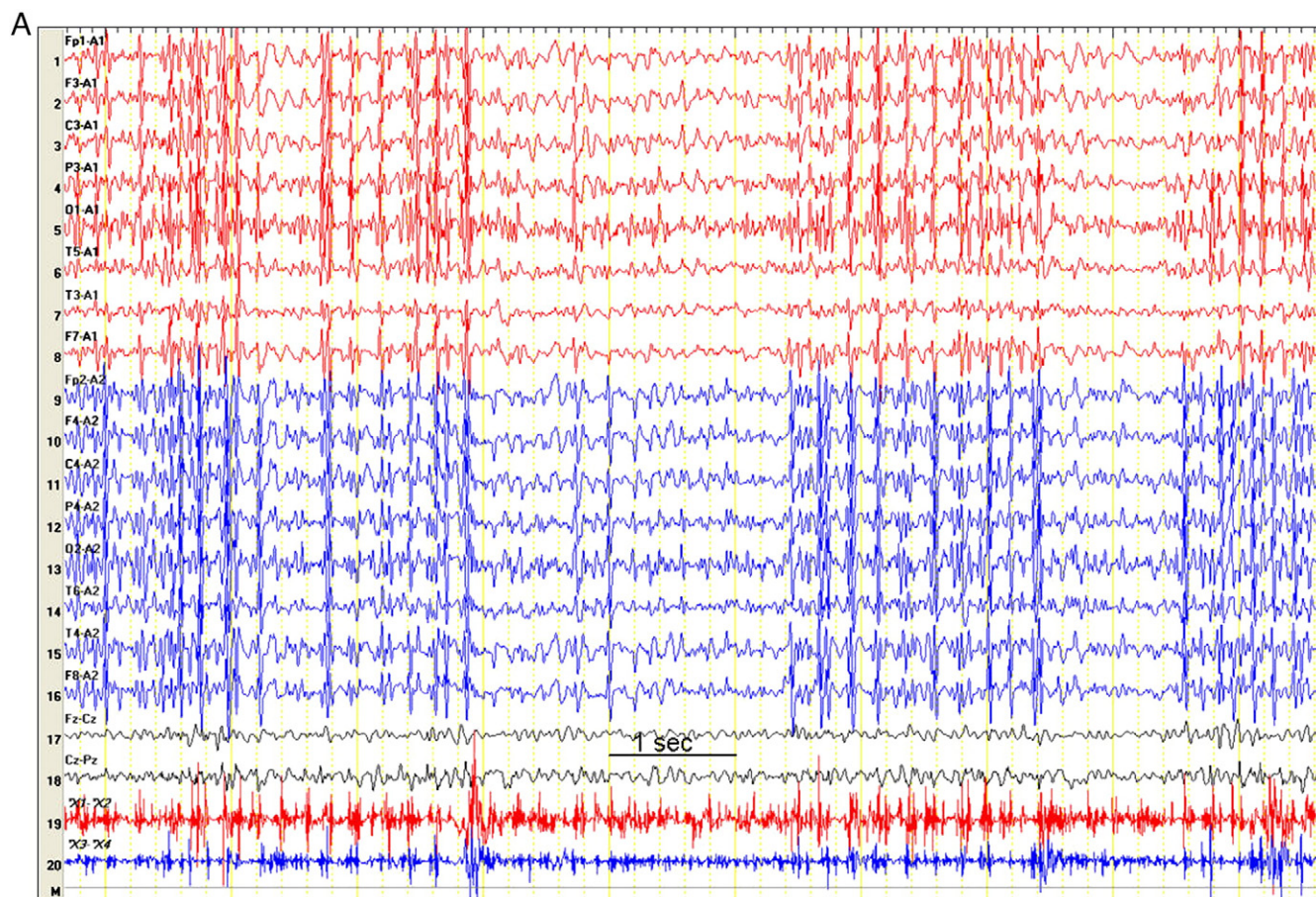


Table 1
Clinical and EEG features of the patients.

Case (sex and age)	Accompanying disease	Possible cause of MSE	Seizure types	Ictal EEG pattern	Treatment of MSE (mg/day)
1 (M, 84)	Dementia, DM	Quetiapine Genetic predisposition	MSE	Frequent bursts of rapid generalized spikes lasting 1–3 s	DZP (10) i.v., LEV (1000) p.o., quetiapine stopped
2 (M, 78)	AF, subacute ischemic stroke	Not found	MSE	Generalized, 5- to 15-Hz, high-amplitude spikes	DZP (10) i.v., LEV (1500) p.o.
3 (M, 52)	Chronic renal failure, gastric bleeding	Ceftriaxone Uremia Hemodialysis	MSE GTCS NCSE	GPSWD, major increase of ictal activity during IPS	VPA (2000) i.v., ceftriaxone stopped
4 (F, 56)	MM, chronic pain	PGB, antineoplastic agents	MSE	Generalized, frequent 5- to 10-Hz bursts of spikes	LEV (750) p.o., PGB stopped
5 (F, 73)	Ischemic stroke, dementia, neuropathic pain	PGB	MSE	Rapid generalized spikes	PGB stopped
6 (M, 53)	Chronic renal disease, bladder cancer	Meropenem Hemodialysis	MSE	GPSWD, major increase of ictal activity during IPS	DZP (20) i.v., VPA (2000) i.v., LEV (1500) i.v. Meropenem stopped

M (Male), F (Female), DM (diabetes mellitus), AF (atrial fibrillation), MM (multiple myeloma), GTCS (generalized tonic-clonic seizures), MSE (myoclonus status epilepticus), NCSE (non-convulsive status epilepticus), GPSWD (generalized polyspike-and-wave discharges), IPS (intermittent photic stimulation), DZP (diazepam), LEV (levetiracetam), PGB (pregabalin), VPA (valproic acid), BMT (bone marrow transplantation).

Disclosure

None of the authors has any conflict of interest to disclose. We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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References

- [1] Ohtahara U, Ohtsuka Y. Myoclonic status epilepticus. In: Engel J, Pedley T, editors. *Epilepsy. A comprehensive textbook*. 5th edition. Lippincott Ravens; 2008. p. 725–8 [Chp 62].
- [2] Juma-as A, Brenner RP. Myoclonic status epilepticus: a clinical and electroencephalographic study. *Neurology* 1990;40(8):1190–202.
- [3] Engel J. Report of the ILAE classification core group. *Epilepsia* 2006;47(9):1558–68.
- [4] Thomas P, Valton L, Genton P. Absence and myoclonic status epilepticus precipitated by antiepileptic drugs in idiopathic generalized epilepsy. *Brain* 2006;129(Pt 5):1281–92.
- [5] Knake S, Klein KM, Hattemer K, et al. Pregabalin-induced generalized myoclonic status epilepticus in patients with chronic pain. *Epilepsy Behav* 2007;11:471–3.
- [6] Torre JF, Sanchez SC, Pola FC, Calleja J. Stimulus-sensitive post-anoxic focal motor seizures evolving into generalised myoclonic status epilepticus: a video-EEG study. *Epileptic Disord* 2010;12(1):69–72.
- [7] Vollmall C, Noachtar S. Tiagabine-induced myoclonic status epilepticus in a nonepileptic patient. *Neurology* 2007;68(23).
- [8] Larch J, Unterberger I, Bauer G, Reichsoellner J, Kuchukhidze G, Trinka E. Myoclonic status epilepticus in juvenile myoclonic epilepsy. *Epileptic Disord* 2009;11(4):309–14.
- [9] Healy DG, Ingle GT, Brown P. Pregabalin and gabapentin associated myoclonus in a patient with chronic renal failure. *Mov Disord* 2009;24(13):2028–9.
- [10] Jimenez-Jimenez FJ, Puertas I, Toledo-Heras M. Drug induced myoclonus: frequency, mechanisms and management. *CNS Drugs* 2004;18(2):93–104.
- [11] Grill MF, Maganti RK. Neurotoxic effects associated with antibiotic use: management considerations. *Br J Clin Pharmacol* 2011;72(3):381–93.
- [12] Dogu O, Sevim S, Kaleagasi H. Seizures associated with quetiapine treatment. *Ann Pharmacother* 2003;37:1224–7.
- [13] Niedermeyer E. Metabolic central nervous system disorders. In: Niedermeyer E, Lopes Da Silva F, editors. *Electroencephalography: basic principles, clinical applications, and related fields*. fifth edition. Lippincott Williams & Wilkins; 2005. p. 443–4 [Chp 22].
- [14] Gastaut H. Classification of status epilepticus. *Adv Neurol* 1983;34:15–35.
- [15] Treimen DM. Generalized convulsive status epilepticus in the adult. *Epilepsia* 1993;34(Suppl. 1):S2–S11.

Fig. 1. A: EEG recordings from patient 1 on monopolar montage showing very frequent bursts of rapid generalized poly-spikes with normal background activity. Note that myoclonic jerks correlated with spike activities. (X1–X2 and X3–X4 are surface EMG recordings from extensor muscles of the arms) (Calibration: 1 s per between vertical lines, sensitivity 15 μ V). B: EEG recordings of patient 1 on monopolar montage. After intravenous injection of 10 mg diazepam, epileptic activity was resolved. (Calibration: 1 s per between vertical lines, sensitivity 15 μ V).