Stimulus-sensitive post-anoxic focal motor seizures evolving into generalised myoclonic status epilepticus: a video-EEG study

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ABSTRACT – We describe the case of a 62-year-old man who developed stimulus-induced focal motor seizures after prolonged cardiac arrest. During a video-EEG study, these focal motor seizures progressed into a generalised myoclonic status epilepticus. Both the severely decremented background activity on the EEG, and the absence of median and trigeminal somatosensory evoked potentials were in keeping with a devastating post-hypoxic encephalopathy and the patient died. Our clinical and electrophysiology data suggest that generalised myoclonic status epilepticus may occur in patients in whom the existence of severe cerebral damage prevents a complete development of all phases of classic generalised tonic-clonic seizures. [Published with video sequences]

Key words: stimulus-sensitive post-anoxic seizures, post-hypoxic myoclonus, generalised myoclonic status epilepticus, stimulus-induced rhythmic periodic ictal discharges

Generalised myoclonic jerks are not an uncommon clinical feature in patients with severe post-hypoxic encephalopathy. However, the exact pathophysiology continues to be discussed. While some authors believe that post-anoxic myoclonus likely arises from a brainstem generator since a severely damaged cortex is unlikely to be the origin (Hallet, 2000), others have reported findings supporting the hypothesis that it represents a genuine epileptic state (Celesia et al., 1988; Jumao-as and Brenner, 1990; Van Cott et al., 1996).

In this study, we describe the video-EEG findings of a patient who experienced stimulus-induced focal motor seizures progressing into a generalised myoclonic status epilepticus (GMSE), suggesting a close relationship between both epileptic conditions.

Case study
A 62-year-old man was admitted to our hospital after resuscitation from acute cardiopulmonary arrest. He had antecedents of hypertension and his father’s...
death had been sudden and unexpected. Based on neurological examination, the man was comatose without response. The pupils were mydriatic and unreactive, brainstem reflexes were absent and plantar responses were extensor bilaterally. Over the following hours, he experienced massive generalised myoclonic jerks. At that moment, treatment with valproic acid (1,500 mg/24 h) was started.

Twenty-four hours after admission, the mental state of the patient remained unchanged with only occasional body jerks. An EEG was subsequently requested; it should be noted that v-EEG is routinely performed for all our patients admitted to the intensive care unit using a portable digital Micromed electroencephalographer. V-EEG showed background activity consisting of low voltage diffuse alpha-theta activity, suggestive of a severe anoxic encephalopathy (figure 1). During this recording session, painful stimulation provoked rhythmic clonic twitching in the right hand which progressively evolved into massive generalised myoclonic jerks. This episode lasted for two minutes and finally ceased after administration of 0.5 mg of clonazepam. Frank, well-formed generalised low voltage spikes and spike-and-wave complexes with left-sided emphasis were associated with generalised myoclonia (figure 2). Twenty four hours later, a second v-EEG revealed a nearly flat recording without evidence of epileptiform discharges. During the first part of the recording, the patient remained immobile. When the technician carried out painful stimulation on the right nipple, rhythmic clonic movements of the right hand were
provoked (see video sequence 1). These motor manifestations were associated with transient stimulus-induced bilateral low-voltage rhythmic spikes, more accentuated over the left hemisphere (figure 3A, B). These EEG changes were compatible with stimulus-induced rhythmic periodic ictal discharges (SIRPIDs). The passive mobilization of the right arm also enhanced right rhythmic jerks (see video sequence 2). The painful stimulation of the contralateral nipple increased right hand jerks and also provoked very brief and transient clonic movements affecting the left leg and, on other occasions, proximal segments of both upper limbs (see video sequences 3 and 4). Isolated subtle clonic movements of the right hand persisted for seconds to minutes and intensity diminished slowly and progressively (see video sequence 5). Finally, bilateral stimulation over both trigeminal areas significantly increased right hand clonic movements and precipitated the appearance of myoclonic jerks in the proximal segments of the upper limbs and trunk, which were associated with bilateral low-voltage rhythmic negative spikes (figure 4; see video sequence 6). These motor manifestations persisted for at least 10 minutes and always increased with trigeminal and painful stimuli. During these periods, rhythmic generalised epileptiform discharges increased in frequency and amplitude on the EEG. Under these circumstances, clinical and EEG features were compatible with the diagnosis of massive generalised myoclonic status epilepticus (figure 5A, B; see video sequence 7). Intermittent photic stimulation did not significantly modify clinical and electroencephalographic features. To confirm the epileptic origin of the EEG anomalies, an intravenous bolus of 4 mg of clonazepam was administered which suppressed motor manifestations and generalised epileptiform discharges (figure 5C). To complete the electrophysiological evaluation, median and trigeminal evoked potentials were carried out. Cortical evoked responses were absent bilaterally. Unfortunately, neuroimaging was not performed. The patient died the day following admission. Necropsy was not authorised.
Discussion

Stimulus-sensitive seizures, including partial motor, clonic, myoclonic and generalised tonic-clonic, have been rarely described in the past in subjects with post-anoxic coma (Niedermeyer et al., 1977; Van Cott et al., 1996; Gatzonis et al., 2001; Zivkovic and Brenner, 2003; Fernández-Torre et al., 2005; Fluri et al., 2008; Hirsch et al., 2008). Our case study provides further clinical and EEG data to better understand the pathophysiology and relationship between acute post-hypoxic myoclonus and partial and generalised seizures. To the best of our knowledge, this case offers, for first time, the opportunity to observe a detailed video-EEG study of a relatively unusual epileptic phenomenon. Reflex focal motor seizures were elicited by somatosensory stimulation. The duration, maintained rhythmicity and the lack of a shock-like component supports this nosologic classification. Clonic movements of the right hand were accompanied by bilateral epileptiform discharges more accentuated over the left hemisphere. The existence of bilateral changes, despite unilateral motor symptoms, has been also mentioned by others in similar situations (Gatzonis et al., 2001). This clinico-electroencephalographic dissociation may be a consequence of non-uniform widespread damage in structures involved in the propagation of epileptic activity. The presence of asymmetric epileptiform discharges which had higher amplitude on the left hemisphere could suggest more severe injury on the right side. Moreover, focal motor seizures progressed into massive and generalised myoclonic jerks constituting a definitive picture of GMSE. Therefore, our findings support the hypothesis defended by other authors, suggesting that GMSE might represent a genuine epileptic state (Celesia et al., 1988; Jumao-as and Brenner, 1990; Van Cott et al., 1996). The rhythmic progression of the electroencephalographic pattern and response to the administration of rapid action antiepileptic drugs supports this affirmation.

Kanemoto and Ozawa (2000) described the occurrence of non-cortical generalised myoclonic jerks and alternating cortical jacksonian seizures in the same individual. In contrast, in the case reported here, despite a severe depression of background activity, somatosensory stimuli elicited partial motor seizures which evolved into GMSE of cortical origin. Both situations seem possible in the context of anoxia and, therefore, an EEG is essential to make an adequate distinction.

Although the clinical correlate of SIRPIDs has not yet been completely delineated, it refers mostly to comatose patients showing no motor signs. Indeed, in the paper by Hirsch et al. (2004), only one patient demonstrated motor manifestations associated with the occurrence of SIRPIDs. However, recently, Fluri et al. (2008) described a case somewhat similar to our patient in which SIRPIDs were associated with a clearly evolving electrographic generalised seizure pattern induced by tactile stimulation, exclusively of the ophthalmic nerve. The evolving pattern was accompanied by bilateral periorcular twitching. A diagnosis of post-anoxic generalised status epilepticus was considered. As commented by these authors, acute stimulus-sensitive post-anoxic myoclonus has been rarely observed in relation to different types of stimuli, such as passive eye opening and closing and trigeminal and nipple stimulation (Niedermeyer et al., 1977; Gatzonis et al., 2001; Zivkovic and Brenner, 2003; Fernández-Torre et al., 2005). Moreover, Hirsch et al. (2008) have also described the occurrence of focal motor seizures consistently elicited by alerting stimuli in severely ill patients. These ictal manifestations, also noted for our patient,
Figure 5. Fragments of the EEG showing the progression into a generalised myoclonic status epilepticus (GMSE). A) Intermediate phase with moderate clinical and electroencephalographic manifestations. B) Massive generalised myoclonic jerks in keeping with a severe GMSE. C) Abolition of epileptiform discharges after the administration of 4 mg of intravenous clonazepam (arrow).

Low filter: 0.33 Hz; High filter: 70 Hz; Notch filter: 50 Hz. Vertical bar: 50 μV. Horizontal bar: 1 second (speed 15 mm/s).
were stimulus intensity-dependent because they persisted and increased in severity when stimulation was sustained. SIRPIDs were evoked after painful and tactile stimuli. Although these EEG abnormalities have been thoroughly described recently, their significance remains unresolved (Hirsch et al., 2004). In our case, some of these epileptiform discharges were associated with clonic contractions of the contralateral upper limb, indicating an ictal nature. In addition, repetitive sensory stimuli converted transient rhythmic discharges into a genuine pattern of GMSE. It seems, therefore, that at least in the case reported here, SIRPIDs constitute an onset ictal pattern. These findings support the hypothesis of Koutroumanidis et al. (2008) who suggested that these phenomena may represent reflex seizures of the critically ill.

In summary, in order to carry out different types of stimuli during the EEG recording in comatose subjects is a crucial step for detecting both SIRPIDs and reflex clinical seizures.

Moreover, the possibility that reflex partial motor seizures may evolve into GMSE in patients with severe cortical damage supports the hypothesis that post-anoxic myoclonus represents an ictal state of epileptic nature. Moreover, our case supports the concept proposed by Celesia et al. (1988) suggesting that GMSE represents a fragmented epileptic state because it occurs in patients in whom the existence of severe cerebral damage prevents the complete development of all phases of classic generalised tonic-clonic status epilepticus.

**Disclosure.**

None of the authors has any conflict of interest to disclose.

**References**


