

## Case Report

## A case of ictal burst-suppression

Pegah Afra<sup>a,b,\*</sup>, Verena Clarissa Samara<sup>b</sup>, Lilly Fagatele<sup>b</sup>, Bola Adamolekun<sup>c</sup><sup>a</sup> Department of Neurology, Weill-Cornell Medicine, NY, USA<sup>b</sup> Department of Neurology, School of Medicine, University of Utah, UT, USA<sup>c</sup> Department of Neurology, University of Tennessee Health Science Center, TN, USA

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## ABSTRACT

“Burst-suppression” pattern consists of complete attenuation of background between bursts of mixed frequencies, variable morphology and waveforms. It is a subgroup of periodic patterns seen in severe cerebral damage, anesthesia or prematurity. Here, we present a 46-year-old woman with post-anoxic encephalopathy on cooling protocol with two electrographically similar patterns of burst-suppression (one with a clinical ictal correlate of isolated eye movements), as well as three electroclinical seizures. The literature on rare clinical phenomenon of isolated eye movements associated with burst-suppression is reviewed, with the conclusion that the presented case suggests an ictal origin.

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## 1. Introduction

The burst-suppression pattern is a subgroup of periodic patterns on EEG in which there is complete attenuation of background activity (suppression or inter-burst intervals) in between bursts of 0.5 s or longer in duration [1]. The bursts consist of mixed frequencies, variable morphology, and variable waveforms including sharp waves and spikes [1]. This pattern is very commonly seen in intensive care units in patients with severe cerebral damage including post-anoxic encephalopathy, and during anesthesia and in prematurity [2–5].

In this case report, we present a patient with post-anoxic encephalopathy who showed two burst-suppression patterns that are similar with regard to the burst and inter-burst interval duration but differ in regard to clinical features. One burst-suppression pattern was associated with a clinical ictal correlate and therefore referred to here as an “ictal burst-suppression” pattern; and the other pattern occurred after optimization of pharmacologic suppression with no clinical correlate and therefore referred to here as “therapeutic burst-suppression”.

## 2. Materials and methods

## 2.1. Patient

Our patient was a 46-year-old woman with a past medical history of substance abuse, hypertension, and depression, who was in her normal

state of health until her family heard a “thump” one early morning and found her unresponsive in the bathroom. CPR was started immediately by her family and continued for about 30 min before the emergency medical service (EMS) arrived. After administration of epinephrine, the patient had return of autonomous circulation and demonstrated spontaneous movements. Her estimated glasgow coma scale (GCS) at the scene was 3. She was taken to the nearest emergency room (ER), where a CT head showed no acute abnormalities. She was then transferred to the University of Utah Medical Intensive Care Unit. On arrival she was started on a vascular cooling protocol and monitored with continuous video-EEG.

## 2.2. Methods

## 2.2.1. Continuous video-EEG

Nineteen scalp electrodes were placed according to the 10–20 system of electrode placement and digital EEG was recorded using the XLTEK EMU 40 system (Natus Medical Inc., Middleton, WI) with a sampling rate of 250 Hz, low frequency filter of 1 Hz, high frequency filter of 70 Hz and notch filter of 60 Hz were applied. Video-EEG data were analyzed off-line and display montage was adjusted as needed.

## 2.2.2. MR imaging acquisition protocol

MRI was acquired with a 1.5 T MR scanner (Siemens, Erlangen, Germany) and sagittal MPRAGE, coronal T1, T2, post FLASH, MPR, and TRUE IR and axial T1, T1 post WE, T2, T2 post, FLAIR, DWI, GRE sequences were obtained.

\* Corresponding author at: Department of Neurology, Weill-Cornell Medicine, NY, USA.  
E-mail address: [pea9031@med.cornell.edu](mailto:pea9031@med.cornell.edu) (P. Afra).

### 3. Results

#### 3.1. Clinical course and video-EEG monitoring

The patient reached a goal temperature of 35° at 1 h and 15 min after starting cooling protocol with an arctic sun device. She was cooled for 24 h and then rewarmed to normal body temperature over the following 48 h.

The EEG showed abnormal bursts of medium to high amplitude sharp waves in theta-low alpha frequency lasting 0.5–2 s in duration with a clinical correlate of slow eye-opening that was followed by a blink time-locked to the EEG bursts, and therefore were considered “ictal bursts” (Fig. 1-A). The inter-burst intervals consisted of completely suppressed EEG and were variable in duration, lasting 4 s to 4 min with no clinical correlate. There were no eye movements or any other clinical movements during the inter-burst intervals. There were three bursts that were followed by electro-clinical seizures of up to 25 s in duration (Fig. 1-B), consisting of rhythmic delta intermixed with theta frequencies (i.e. three seizures total). The only clinical correlate to these electro-clinical seizures was slow eye opening at ictal onset with intermittent eye blinks or eye flutter.

The patient had been started on continuous IV propofol and midazolam as part of a vascular cooling protocol. The dosages were increased and adjusted until the “ictal burst-suppression” slowly transitioned to “therapeutic burst suppression”, with similar burst duration but no clinical correlate (Fig. 1-C). After increasing the IV propofol and midazolam there were no further electroclinical seizures. Shortly thereafter, the “therapeutic burst-suppression” evolved into near complete suppression for the remainder of the first day. It was not possible to know for sure if the anesthetic effect of propofol and midazolam suppressed the movements or electroclinical seizures. Additionally IV levetiracetam 3000 mg/day and IV lacosamide 400 mg per day in divided bid doses were added. On the second day (26 h following onset of video-EEG recording) the patient’s EEG transitioned into generalized periodic discharges (GPDs, Fig. 1-D). After obtaining the MRI report (see below), the patient’s family was counseled regarding an anticipated poor prognosis and care was discontinued on the third day after presentation.

#### 3.2. MRI results

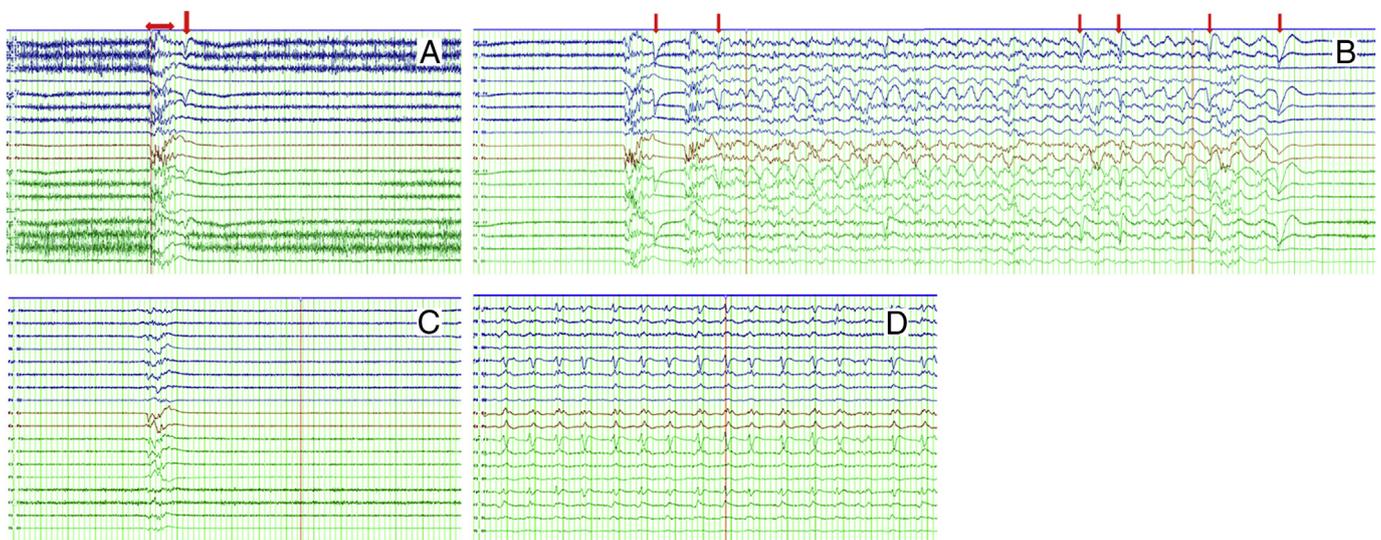
An MRI, done 84 h after the patient was found (72 h after admission) demonstrated mildly increased FLAIR signal within the extra-axial spaces bilaterally (Fig. 2-A, B) as well as diffusion restriction in the bilateral basal ganglia and the entire cortical ribbon (Fig. 2-C, D, E), consistent with global anoxic injury.

### 4. Discussion

The MRI in the presented patient is consistent with a severe post-anoxic encephalopathy, a devastating condition with distinctive MRI findings [6]. During the acute and early subacute phases, increased signal is seen in the cortex, thalamus, and basal ganglia on both DWI and T2-weighted sequences as the gray matter is more vulnerable to hypoxia than white matter. These later fade and diffuse white matter abnormalities develop, followed by diffuse atrophy [7]. In addition to clinical findings and neuroimaging, EEG has been used as a tool for prognostication after hypoxic brain injury. Several EEG patterns can be observed ranging from mild, non-specific slowing to burst suppression patterns and electrocerebral inactivity, reflecting increasing degrees of cerebral dysfunction [8].

Ictal activity including GPDs is seen in up to 35% of post-anoxic patients monitored with EEG [9]. The presence of ictal activity or clinical seizures indicates that cortical structures are severely but incompletely damaged, making them predictors of poor outcome [10,11]. Ictal activity is usually seen in the form of non-convulsive status epilepticus (SE) or myoclonic SE. In the latter case, EEG can show generalized periodic discharges or burst-suppression pattern with the bursts synchronized with clinical myoclonic jerks. Hallet suggested that the acute post-hypoxic myoclonus likely arises from a brain stem generator, because the cortex is severely damaged and not capable of generating activity; and because generalized jerks are characteristic of a brain stem origin [12].

Reeves et al. [13] considered a variety of pathophysiologic mechanisms underlying the phenomenon of burst-suppression associated with movements (including eye movements), depending on the temporal relation to the bursts and the movements itself. These included: a) complex sequence of non-myoclonic movements (such as chewing, swallowing) related to motor programs at the



**Fig. 1.** EEG patterns (Sensitivity 10  $\mu$ V/mm, LFF: 1 Hz, HFF 70 Hz, Notch 60 Hz); Standard bipolar montage: Blue: right hemispheric channels (lateral on top of paracentral channels); Red: central channels; Green: left hemispheric channels (lateral on top of paracentral channels). A) Ictal burst suppression. The horizontal arrow marks slow eye opening which is followed by an eye blink (vertical arrow). B) Ictal burst followed by an electroclinical seizure (tonic eye opening followed by intermittent eye blinks (vertical arrows)). C) Therapeutic burst suppression. D) Evolution of GPDs.

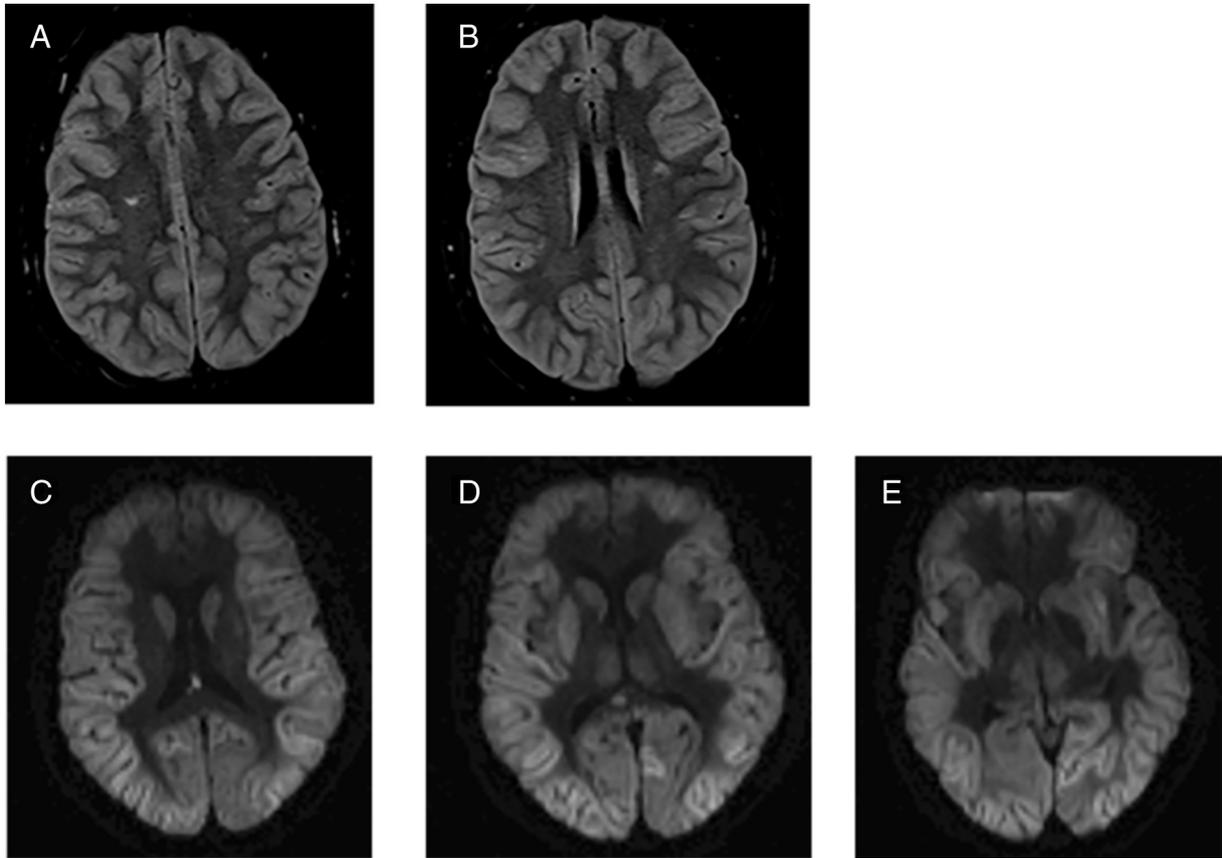


Fig. 2. Illustration of the patient's MRI. FLAIR hyperintensities in the bilateral centrum semiovale (A, B). Diffuse cortical diffusion restriction on DWI (C, D, E).

brain stem or subcortical level; b) movements that occur exclusively between bursts (i.e. during interburst intervals) which were considered to be brain-stem release phenomenon; and c) fragmentary movements during bursts including focal or generalized myoclonus that reflect cortical activity with excitatory influence on subcortical motor neurons (i.e. ictal phenomenon). Our patient's case is similar to this last category in that the bursts had a clinical correlate, although her eye movements were not myoclonic in nature and consisted of slow eye opening ending in a blink. Therefore we use the term “ictal burst-suppression” to described the electroclinical finding.

Eye movements associated with burst-suppression are a rare but well described clinical phenomenon. We have summarized the existing clinical literature in Table 1 [13–21]. Of the 25 existing cases in the literature, nine are exclusively eye movements with no other signs reported accompanying the movements and therefore closely resemble our case. Some authors [13,15,21] considered ictal causes in the differential of their reported patients, while other authors [14,16–20] considered the eye movements not to be ictal in nature and/or to be of brain stem origin.

Our case is electro-clinically different from most reported cases for two reasons. Firstly, during ictal burst suppression, we had

Table 1

List of existing case series and case reports that include eye movement associated with burst suppression.

Case report/series	Cases with eye movements (EM)	Isolated EM or not isolated EM	Reported EEG characteristics: TRB; EM artifact	Associated GTC	Proposed mechanism
Wolf 1977	4/5 cases	Not isolated	TRB	No mention	Brain stem origin
McCarthy and Marshall 1981	4/5 cases	4/5 Isolated	TRB	No mention	Not clear (convulsive versus release phenomenon)
Mori et al. 1983	1 case	Not isolated	TRB	Uncontrollable GTC for 24 h prior	Sign of structural or functional derangement of subcortical gray matter
Jordan et al. 1982	1 case	Not isolated	TRB, no EM artifact	No mention	Not stated
Reeves et al. 1997	12 cases	1/12 Isolated 11/12 Not isolated	TRB	No mention	Multiple mechanisms suggested include ictal causes (please see text)
Fernandez-Torre 2008	1 case	Not isolated (Followed by swallowing movements)	TRB (EO at the onset of the burst and EC at the conclusion of the burst)	2 GTC on presentation	Not seizure; cortex is too damaged to have centrifugal activity; recurrent activation of thalamic networks
Ferrara 2012	4 cases	2/4 Isolated 2/4 Not isolated	TRB (rapid EO at the onset of the burst; slow EC coincided with periods of suppression)	No mention	Transient phenomenon heralding rostrocaudal deterioration in BS function
Crawford 2012	1 case	Isolated	TRB-EM occurred at the conclusion of burst	No mention	Release phenomenon due to diffuse hypoxic-ischemic injury
Dericioglu 2014	1 case	Isolated	TRB	No mention	Ictal causes considered in differential diagnosis

EM eye movements; TRB temporally related to bursts in burst-suppression EEG; GTC generalized tonic clonic seizure; EO eye opening; EC eye closure.

electrographic evidence of the eye-blink artifacts time-locked to the EEG bursts (0.5–2 s in duration), pointing to the fact that the clinical accompaniment of slow eye opening followed by a blink occurred only during the bursts. There were no associated movements during the inter-burst intervals. Secondly, the emergence of three electroclinical seizures consisting of prolonged bursts lasting up to 25 s with clinical accompaniment of slow eye opening followed by intermittent eye blinks were very similar to other ictal discharges in bursts that were no longer than 2 s. Apart from these three recorded seizures, our patient did not have any other clinical seizures and her EEG pattern was not part of the evolution of status epilepticus.

The above two electro-clinical correlations are highly suggestive of an ictal etiology for the eye movements associated with bursts in this case, hence our use of the term “ictal burst-suppression”. We acknowledge the possibility of a brainstem facilitated slow eye movement for this case's presentation (i.e. a subcortical or brain stem etiology independent of cortical discharge). However we think that the temporal and clinical correlation of abnormal eye movements to the bursts and to the electroclinical seizures reflects the influence of excitatory activity over the involved pathways and therefore support an ictal origin generated by the cortex.

## 5. Conclusion

Isolated eye movements associated with burst-suppression are rare clinical phenomena that are well described in the literature with the majority of authors considering eye movements to be of brain stem origin. We present a case of isolated eye movements suggestive of an ictal origin and conclude that in cases of post anoxic encephalopathy with burst-suppression pattern, an ictal etiology should be considered when isolated eye movements are seen in a time-locked fashion to the EEG bursts. The burst-suppression following cardiac arrest is associated with a poor prognosis. The finding of associated isolated clinical eye movement, (regardless of their ictal and cortical origin or a subcortical/brain stem generator) does not change the overall poor prognosis associated with this clinical sign.

## Conflict of interest

The authors have no conflict of interest.

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