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Tonic Eye-Opening Associated with the «Burst-Suppression» Pattern in Patients with Acute Anoxic Brain Injury (Case Series)

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Summary

Massive anoxic brain injury caused by cardiac arrest leads to wakefulness suppression up to coma. The prediction of outcome is based on the analysis of the clinical features and the results of instrumental tests. One of the well-known signs of an unfavorable prognosis is involuntary motor activity, which is most commonly represented by myoclonus. In case of their cortical origin, they are accompanied by epileptiform activity in the electroencephalogram (EEG).

Material and methods. We present a case series and literature review concerning a very rare fatal sign, nonrhythmic spontaneous eye opening accompanied by a «burst-suppression» pattern (BS) in the EEG. All patients suffered from transient acute hypotension or arrhythmia that required cardiopulmonary resuscitation (CPR) in three cases. A literature search found only 11 publications describing post-anoxic tonic eye-opening (PATEO).

Results. The PATEO with BS was observed for less than a day followed by cessation of brain bioelectric activity in all patients. Only two patients exhibited isolated eye-opening and closing, while the rest had axial and limbs myoclonus just after CPR. In one case, eyelid opening was followed by a clonic movement of the head to the right, the EEG bursts were prolonged and had spike-like morphology. Three patients received antiepileptic and sedative therapy. All patients died in 3–43 days after the fatal cardiovascular event.

Visual superposition of bursts in EEG and myogram of m. orbicularis oculi demonstrating identical morphology for EEG and myographic bursts was described for the first time. Our cases and literature review confirm that, regardless of the intensive treatment, patients with PATEO have fatal outcomes.

Conclusion. The clinical and electrographic PATEO with BS phenomenon always indicates a lethal prognosis. The origin of PATEO is still under discussion. We suggest that it could be caused by disinhibition of subcortical and stem structures during extensive death of cerebral cortical neurons.

Key words: EEG; burst-supression; myoclonus; anoxia

Conflict of interest. The authors declare no conflict of interest.

Introduction

Prognostication in coma is essential for selecting an intensive care strategy [1]. For this purpose, both clinical signs and instrumental methods of central nervous system investigation such as computed tomography (CT), electroencephalography (EEG), somatosensory evoked potentials (SSEPs) are used. Beyond pharmacologic sedation, complete cessation of any motor activity or myoclonus indicates severe brain damage and a poor prognosis for recovery of consciousness [2]. In contrast, motor seizures and other manifestations of motor activity are not associated with a fatal outcome and are a positive prognostic factor, reflecting preserved cerebral function [3]. Spontaneous and reflex movements observed in brain death are distinct, but the location of active myotomes below the C2 spinal segment is their obligatory feature [4].

We observed five patients in deep coma after acute anoxic brain injury with a rare and unusual sign, isolated slow eyelid opening and closing, which lasted for several dozen hours consecutively and was followed

by a fatal outcome regardless of the chosen intensive therapy approach. Simultaneously, the EEG recorded a burst suppression pattern (BSP), in which the bursts occurred synchronously with the onset of upper eyelid movement. We present a summary of patient histories and a review of publications confirming that postanoxic tonic eyelid opening (PATEO) is a poor clinical and EEG prognostic sign indicating an extremely high probability of fatal outcome. The methodology of data analysis and presentation was approved by the local ethics committee of the N.V. Sklifosovsky Research Institute for Emergency Medicine.

Materials and Methods

Case 1. Patient D., 57 years old, was admitted to the clinic of the Federal Medical and Biological Center named after Burnazyan of the Russian Federal Medical and Biological Agency for surgical treatment of gastric tumor. On the first day after the surgery, which included subtotal distal gastric resection with creation of gastroenteroanastomosis, the patient developed massive intra-abdominal bleeding, which was controlled by repeated surgical intervention. Due to severe hypotension caused by hemorrhagic shock, coma developed along with respiratory failure requiring mechanical ventilation, while no cardiac dysfunction or arrhythmias were noted. The patient remained in critical condition the next day. Neurological status: muscular atonia, total areflexia, GCS score of 3, FOUR score of 1. Severe generalized myoclonus of the body and limb muscles accompanied by periodic opening/closing of the eyelids with a frequency of about once every 8–10 seconds. This was considered a manifestation of myoclonic epileptic status, and drug therapy with sodium thiopental was initiated, during which the myoclonus completely resolved, but the slow spontaneous opening/closing of the eyelids persisted for 24 hours, and the eyeballs remained immobile. Video-EEG monitoring, started simultaneously with thiopental infusion, showed that bioelectrical activity of the brain was represented by BSP with the same morphology of bursts with amplitude reaching 200–300 μV, duration varying in the range of 2–10 seconds, and intervals between bursts ranging from 8 to 10 seconds. All EEG bursts were accompanied by eyelid opening and closing (Fig. 1).

This EEG pattern persisted until death, which occurred on the third day after the initial onset of signs and symptoms.

Case 2. Patient N., female, 33 years old, was admitted to the emergency department of A. K. Yeramishantsev City Clinical Hospital with suspicion of ectopic pregnancy. Laparoscopic tubectomy with abdominal drainage was performed. Total blood loss was about 25% of circulating blood volume, blood transfusion was performed with stabilized systemic hemodynamics. The sedated and ventilated patient was transferred from the operating room to the intensive care unit and later extubated. Ten hours after surgery, the patient suddenly developed asystole and cardiopulmonary resuscitation (CPR) was immediately initiated. Spontaneous sinus rhythm was restored after 11 minutes of resuscitation, with no evidence of myocardial ischemic injury on ECG. The patient's condition remained critical, she was in deep coma with stereotyped brief eyelid opening/closing with upward deviation of the eyeballs, repeated every 20 seconds. The patient was started on valproic acid 900 mg daily, and considering the resistance to increasing doses of propofol, sodium thiopental 40 mg/h was added with gradual increase up to 100 mg/h. After initiation of anticonvulsant therapy, EEG monitoring was initiated. The burst suppression pattern was recorded with paired bursts occurring with eyelid opening and partial lowering (the first component of the burst) and repeated eyelid opening at the time of the second component. Both lid openings were accompanied by upward eye deviation, and all bursts had the same morphology. To rule out artifactual origin of EEG bursts due to the patient's eyelid opening, a muscle relaxant trial was performed. Administration of rocuronium abolished the clinical manifestations but did not alter the EEG picture. When the dose of sodium thiopental was decreased, the duration of bursts increased to 20–30 seconds and their amplitude reached 400 μV, and when the dose was increased, paired bursts were transformed into single bursts of about 1 second duration. At the end of the second day after CPR, the bioelectrical activity of the brain was reduced to a minimum, with an amplitude of 2–4 μV. Sedation was discontinued, but PATEO did not resume.

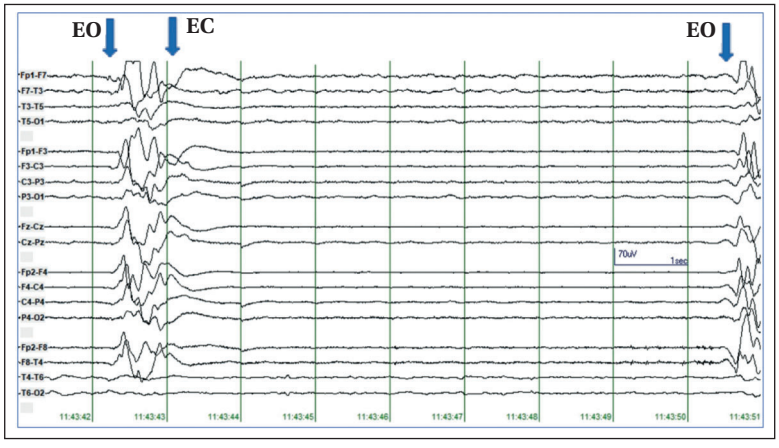

Fig. 1. EEG of patient D. Spontaneous eyelid opening during EEG bursts.
Note. Vertical arrows indicate eyelid opening (EO) and closing (EC).

The disease was later complicated by infection with progressive multiple organ failure, and death occurred on the 43rd day of hospitalization.

When analyzing the EEG of patient N. we first used the EegRev viewer (developed by A.G. Brutyan) to superimpose several bursts in the BSP. The result of processing, demonstrating complete similarity of morphology of EEG and EMG elements at the moment of PATEO, is shown in Fig. 2.

Case 3. Patient B., female, 52 years old, was admitted to the Interregional Clinical and Diagnostic Center, Kazan, with the diagnosis of dissecting aneurysm of the ascending aorta. Prosthetic repair of the ascending aortic hemi-arch was performed under cardiopulmonary bypass. Respiratory failure with low oxygenation requiring prolonged mechanical ventilation developed after surgery. On postoperative day 12, in addition to respiratory failure, acute hypotension and ventricular fibrillation occurred, requiring cardiopulmonary resuscitation, which resulted in cardiac rhythm recovery and hemodynamic stabilization. Impaired consciousness progressed to deep coma and the patient had myoclonic contractions of upper and lower limb and trunk muscles with EEG showing generalized spike-like bursts followed by polymorphic slower impulses lasting 2.5–3 seconds. The patient's condition was diagnosed as nonconvulsive status epilepticus and treatment with sodium thiopental 340 mg/h was initiated. After 4 hours, with continued thiopental infusion, the burst-suppression pattern appeared, with tonic eyelid opening and closing lasting up to 3 seconds between bursts, with episodes of suppression on the EEG lasting up to 10 seconds (Fig. 3). The myoclonus ceased. The PATEO phenomenon was observed continuously for 4 hours, then the eyelid opening/closing gradually stopped and the morphology of the bursts changed from sharper waves to slow-wave theta-band activity. Twenty-four hours after CPR, the last burst of theta waves with an amplitude of up to 20 μV was recorded, and for the next 20 hours there was no electrical activity of the brain. Asystole occurred at 44 hours after CPR.

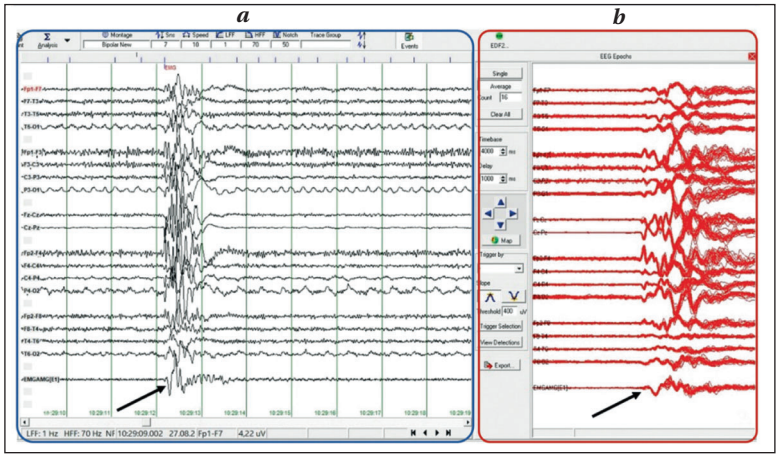

Fig. 2. Electroencephalogram of patient N. as seen in the EEG viewer EegRev. Longitudinal bipolar double banana montage, with myogram registration from the circular muscle of the left eye.
Note. *a* — Native recording, BSP; *b* — Superimposition of 16 bursts showing the same morphology of EEG and muscle contractions (indicated by an arrow).

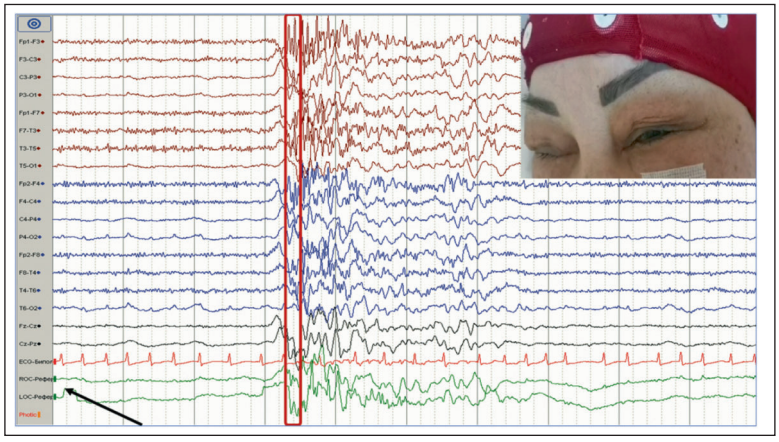

Fig. 3. EEG of patient B. Longitudinal bipolar double banana montage, with myogram registration from the circular muscle of both eyes.
Note. The oculographic channels are indicated by an arrow. The inset shows the beginning of the burst accompanied by the opening of the eyelids. The right eyelid opened less due to edema.

Case 4. Patient M, 89 years old, was admitted to the Sklifosovsky Research Institute for Emergency Medicine after a cerebral infarction of the left middle cerebral artery, and due to a coronavirus infection she was admitted to the ICU of the Infectious Diseases Department of the Institute. She received antihypertensive, antibacterial, and fluid therapy and prophylaxis of thromboembolic and infectious complications. A chest CT scan revealed progressive lung involvement with increasing respiratory failure. Ventilation was started and an inferior tracheostomy was performed. After 6 days, the patient developed right-sided pneumothorax and hydrothorax requiring pleural drainage. The patient's condition progressively worsened, and on the 20th day of hospitalization, cardiac arrest occurred, and cardiopulmonary resuscitation (CPR) was started, which resulted in rhythm restoration and hemodynamic stabilization. On the first day after CPR, the patient was in a deep coma (GCS 3, FOUR 0), muscle tone was globally reduced. There was no spontaneous motor activity. Twenty hours after CPR, periodic spontaneous open-

ing and closing of the eyes occurred, accompanied by a brief myoclonic movement of the head to the left. During video-EEG, BSP was recorded with the duration of uniform bursts up to 6 seconds. The moment of slow eyelid opening coincided with the high-amplitude onset of the burst, and the clonic head movement coincided with its low-amplitude segment containing rhythmic sharp waves (Fig. 4).

To rule out ictal origin of the movements, 700 mg of valproic acid was administered intravenously. Since there was no change, the situation was considered a clinical and electrographic manifestation of severe encephalopathy. The next day, spontaneous eye movements and head jerking stopped, and EEG recorded BSP with short monomorphic bursts and interspike intervals of up to 20 seconds. From the next day onward, EEG showed no bioelectrical activity of the brain, deep coma persisted, brainstem reflexes were absent, muscle atonia was seen, and spontaneous breathing stopped. The patient died on the 7th day after CPR.

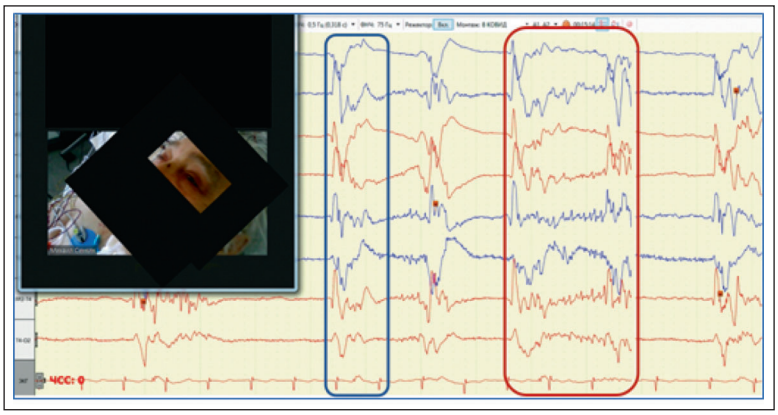

Fig. 4. EEG video window via Zoom application used to communicate with the computer to record the EEG in the infectious ward [5].
Note. The blue frame marks the fragment of the onset of BSP, which coincided with the beginning of eyelid opening, and the red frame marks the clonic rotation of the head to the left.

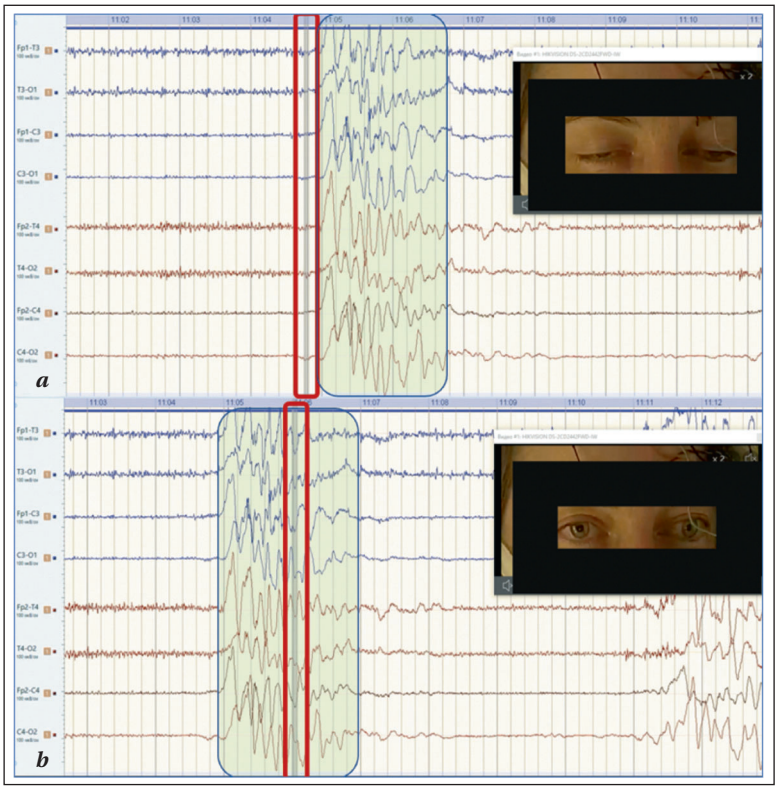

Fig. 5. Video-EEG of patient R. Longitudinal bipolar montage with double interelectrode distance.
Note. *a* — synchronous video recording marker (in the red frame) is set at the interspace, at this moment the patient's eyes are closed; *b* — synchronous video recording marker is set at the center of the flash (highlighted by the green field). The video recording shows a wide opening of the eyes.

Case 5. Patient R., female, 41 years old, with multiple metastatic lesions of the brain and spinal cord, was admitted to the Sklifosovsky Research Institute for Emergency Medicine with a diagnosis of clinical death after a sudden development of coma. Cardiopulmonary resuscitation (CPR) allowed to restore the cardiac rhythm, but the patient's condition remained critical the next day after admission. There was complete areflexia and no muscle tone in the extremities was present. The GCS score was 3 and the FOUR score was 1. Approximately 24 hours after CPR, periodic spontaneous eye opening and closing was noted, which was considered a manifestation of status epilepticus. Continuous EEG recording showed BSP with polymorphic high-amplitude uniform arrhythmic bursts lasting approximately 1.5–2.0 seconds with an interspike interval of 3 to 10 seconds, synchronous with tonic eyelid opening and closing not accompanied by other motor manifestations (Fig. 5).

In the study of somatosensory EPs during median nerve stimulation, no component from the cortical evoked potential response generator (N20–P23 complex) was recorded (Fig. 6).

This was considered as clinical and EEG manifestation of anoxic encephalopathy, therefore anticonvulsants and sedatives were not administered, EEG monitoring was continued. The clinical and electrographic phenomenon lasted for about 20 hours, then the bioelectrical activity of the brain disappeared. There was no subsequent improvement, and death occurred 12 days later due to multiple organ failure.

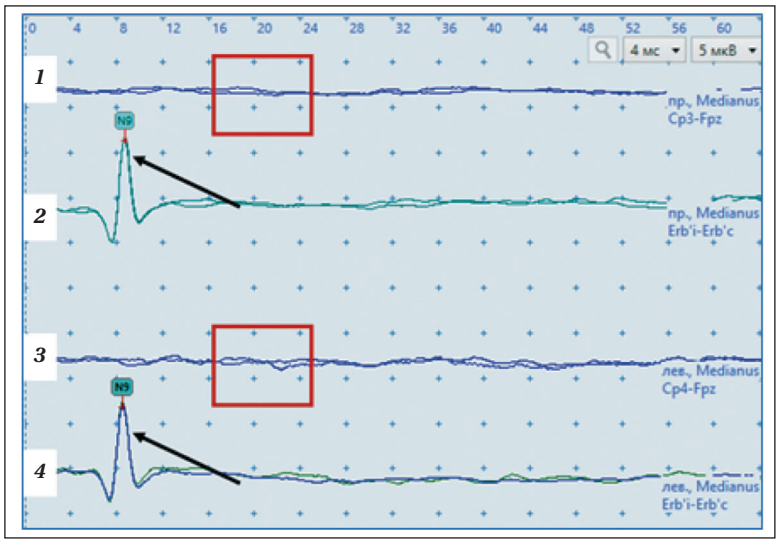

Fig. 6. Somatosensory evoked potentials during median nerve stimulation in patient R.
Note. Traces 1, 3 reflect cerebral leads in the projection of the postcentral gyrus, traces 2, 4 are from Erb points in the projection of the cervical plexus. The arrows indicate the preserved components of the peripheral response 9, the red boxes indicate the presumed location of the missing components N20-P23, reflecting the functional state of the primary sensory cortex.

Thus, all reported cases have in common an unusual clinical sign of tonic eyelid opening and closing in patients with deep areactive coma, which occurred several hours after acute diffuse anoxic brain injury. In all patients, the PATEO phenomenon occurred several hours after CPR, but always within the first day, and its duration did not exceed 24 hours. In one case, eyelid elevation was accompanied by upward deviation of the eyes, and in the other two cases there were synchronous myoclonic jerks of the axial neck muscles leading to head rotation.

All patients showed a specific EEG phenomenon, i. e., BSP with burst onset coinciding with eyelid opening (Table 1).

Discussion

Since verbal contact with the patient in coma is impossible, clinical evaluation is based on the analysis of reflexes and movements, either spontaneous or stimulation-induced. Such motor activity may be a sign of epileptic seizure, delirium, unspecific behavioral changes, disinhibited spinal reflexes in brain death, brainstem herniation, and may indicate an unfavorable prognosis of the disease [6]. EEG recording and analysis of time-related bioelectrical and clinical phenomena is one of the main ways to determine the origin of such movements [7].

We report a well-documented series of cases demonstrating an unusual clinical sign — periodic tonic spontaneous eyelid opening and closing in patients in deep coma caused by acute anoxic brain injury, always accompanied by a burst-suppression pattern on the EEG. The extreme rarity of this phenomenon led to difficulties in the choice of intensive treatment.

A search of the MEDLINE and RSCI databases using the queries «burst suppression,» «postanoxic myoclonus,» «postanoxic myoclonus,» «postanoxic seizures,» «postanoxic movements,» «postanoxic burst suppression,» «postanoxic eye opening,» and «periodic eyelid opening,» and selecting papers describing «eye opening» or «tonic eyelid opening,» yielded 11 publications reporting data from 37 patients with similar clinical and EEG manifestations (Table 2).

The combination of BSP with periodic eyelid opening and closing was first described by P. Wolf in 1977 in a case series of 5 patients with postanoxic encephalopathy who had various spontaneous movements considered to be myoclonus that occurred synchronously with the onset of a burst on the suppressed EEG [8]. In one patient, on day 6 after cardiac arrest and successful cardiopulmonary resuscitation, a nonrhythmic, intermittent, slow raising and lowering of the eyelids lasting approximately 1.5 seconds was observed. This sign was preceded by myoclonus in the axial muscles and limb flexors. The author pointed out that not all bursts in BSP were accompanied by eyelid opening, but when they occurred, they always coincided with a burst of electrographic activity. Two days after the onset of spontaneous eye opening, the patient died.

Table 1. Characteristics of clinical cases.

Clinical case	Age, years	Sex	Specifics	AEDs	Time to death, days
1	57	m	IEO	VA, propofol, thiopental	3
2	33	f	IEO + upward eye deviation	VA, thiopental	43
3	52	f	IEO + myoclonus of limbs and axial muscles	Thiopental	2
4	89	f	IEO + axial neck myoclonus	No	7
5	41	f	IEO	No	6

Note. IEO — isolated eyelid opening; AED — antiepileptic drug; VA — valproic acid.

Table 2. Publications on PATEO with BSP.

No	Author(s)	Number of observations (m/f)	Age, years	Movements other than PATEO	EEG pattern	Time from CPR to death
1	Wolf P. (1977)	1 (0/1)	62	LM, phrenic, mimic, masticatory, tongue AM		2 days
2	McCarty G. E. et al. (1981)	4 (1/3)	4–68	UED, mild decerebrate postural movements in arms of 1 patient		12–24 hours
3	Jordan J. et al. (1982)	1 (1/0)	54	UED, LM in legs not related to BSP	Diffuse slowing after cessation of BSP	28 days
4	Mori E. et al. (1983)	1 (0/1)		GTCSE, AM, UED	Transformation of BSP into GPD after AED administration	Akinetic mutism 1 month after CPR
5	Reeves A. L. et al. (1997)	12 (7/5)	35–90	AM, MK, UED, chewing, tongue protrusions, bobbing		During acute phase of brain injury
6	Fernández-Torre J. et al. (2008)	1 (0/1)	50	Swallowing		5 days
7	Ferrara J. et al. (2012)	4 (3/1)	34–62			Up to 8 days
8	Crawford J. et al. (2015)	1 (1/0)	12			48 hours
9	Dericioglu N. et al. (2015)	1 (0/1)	72	UED	Transformation of BSP into BiIPD	75 days
10	Afra P. et al. (2019)	1 (0/1)	46		Bursts up to 2 s, transformation of BSP into GPD	3 days followed by discontinuation of CPR
11	Alsallom F. et al. (2021)	10 (5/5)	33–74	LM in 4 patients		Up to 7 days

Note. LM — limb myoclonus; AM — axial myoclonus; UED — upward eye deviation; GTCSE — generalized tonic-clonic status epilepticus; AED — antiepileptic drugs; BiIPD — bilateral independent periodic discharges; GPD — generalized periodic discharges.

The first detailed description of slow eye opening and closing synchronous with BSP was published in 1981 by McCarty G. E. et al., who reported 4 patients after cardiopulmonary resuscitation with such isolated stereotypic movements. In all patients, the episode of BSP with eye opening lasted several hours and gradually subsided, followed by cessation of bioelectrical activity on the EEG and death within the next 24 hours. Only one patient had synchronous upward deviation of the eyeballs and mild decerebrate movements that occurred independently of EEG activity. The publication did not indicate whether the patients had received anticonvulsant therapy, but the authors compared the finding to postanoxic myoclonus and noted that it was unclear whether the symptom was a manifestation of the epileptic status or a disinhibition phenomenon due to the termination of central inhibitory influences caused by cortical damage [9].

In a series of 12 cases, Reeves A. L et al. observed more than one type of movement in most patients (92%). Most commonly, there was a combination of PATEO with movements of the face, mouth, and tongue muscles followed by myoclonus, and in two patients more than 4 different types of such movements were observed. In the discussion section, the authors suggested that PATEO with BSP was a manifestation of an epileptic seizure, since the bursts on the EEG reflected cortical activity, with neurons exciting subcortical structures. At the same time, despite antiepileptic treatment administered to half of the patients, all patients reported in the paper died [10].

Among other publications, the description of various movements accompanying the phenomenon of eye opening and closing is quite interesting. For example, Fernández-Torre J. L. et al. described a 50-year-old patient who underwent CPR with rhythm recovery and, in addition to BSP with eyelid opening, had swallowing movements and generalized myoclonus, not always coinciding with the burst in BSP. Rhythmic sharp waves were observed in BSP, and the authors considered this to be an ictal state and administered propofol sedation and anticonvulsants. Despite intensive therapy, the patient died on day 5 after CPR [11].

In a series of 4 observations of BSP with eye opening published by Ferrara J. M. et al, a slight upward deviation of the eyes was recorded in two patients synchronous with their opening. The authors also noted that eye opening ceased in all 4 patients 12 hours after onset, while one of them still had BSP on the EEG, but with a reduced amplitude and frequency of bursts [12].

Eye opening in BSP has not only been observed in adults. For example, Crawford J. R. et al. described this phenomenon in a 12-year-old boy

with anoxic brain damage due to combustion product poisoning [13].

The largest series of observations in patients with PATEO and BSP was reported by Alsallom F. et al. who analyzed video EEG monitoring recordings obtained to predict the progression of coma developing after cardiac arrest. In the series presented, three patients underwent magnetic resonance imaging (MRI) of the brain, which showed relative preservation of the brainstem with significant cortical damage. Because the authors believed that PATEO was an ictal phenomenon, 8 patients were treated with anticonvulsants. Despite this approach, all patients died with a maximum follow-up of 7 days after the onset of PATEO [14].

PATEO with BSP and less fulminant progression. Similar to our observations, all previously published cases of PATEO with BSP were fatal. However, a few publications have described patients with a less pernicious course of postanoxic encephalopathy or with a different electrographic pattern.

In response to the first publication describing PATEO [9], Jordan E. et al. reported a 54-year-old man who underwent CPR followed by generalized myoclonus and then BSP associated with PATEO. Contrary to other observations, the authors pointed out that the day after cessation of PVP, the EEG retained suppressed activity manifested as diffuse slowing, although death occurred on the 28th day after CPR [15].

Dericioglu N. et al. observed a 72-year-old patient with amyotrophic lateral sclerosis who had PATEO with BSP and upward eye deviation on the following day after CPR. It was considered a manifestation of status epilepticus and anticonvulsant therapy was started. Twelve hours later, PATEO ceased and BSP on EEG changed to bilateral independent periodic discharges, which continued with gradual attenuation for over 18 hours. Subsequently, suppressed activity persisted on the EEG, and MRI performed 1 week after CPR showed diffuse damage to the cortex and basal ganglia. Death occurred on the 75th day after CPR [16].

A similar case of «ictal PATEO» was described by Afra P. et al. They reported a 46-year-old female patient with BSP bursts accompanied by EEG-documented epileptic seizures of up to 25 seconds duration. Initial propofol sedation with gradual dose escalation resulted in conversion to BSP with the same burst duration, but PATEO ceased. Decreased sedation with the addition of anticonvulsants resulted in the appearance of the generalized periodic discharge pattern with the same morphology on the EEG. An MRI performed on day 3 showed severe diffuse brain damage, including the basal ganglia, and treatment was discontinued due to the unfavorable prognosis [17].

The only known case of PATEO with BSP in a patient who developed akinetic mutism was published in 1983 by Mori E. et al. A patient with heart failure and atrial fibrillation after cardiopulmonary resuscitation developed a state of generalized tonic-clonic convulsions lasting more than 24 hours, after which rapid eyelid elevation with eye deviation, neck extension, and pupillary hippus remained among the motor manifestations that persisted with anticonvulsant therapy. The movements occurred synchronously with bursts of BSP on the EEG. Over the next 24 hours, the movements ceased and generalized periodic discharges were recorded on the EEG. At the time of publication, the patient was in a state of «akinetic mutism» (corresponding to the modern concept of unresponsive wakefulness syndrome), and there were episodes of alpha rhythm on the EEG [18].

For the first time in the national literature, we described a series of clinical cases of PATEO with BSP. Our observations were in agreement with previously published reports. An isolated oculopalpebral subtype of PATEO was also found in two patients. In one patient, eyelid elevation was accompanied by upward deviation of the eyeballs, and two consecutive bursts corresponding to these movements were registered on the EEG. In another case, PATEO was accompanied by a myoclonic movement of the head to the right, also consistent with published cases. PATEO was observed for a relatively short period of time in all patients, regardless of the life span after CPR, the eyelid movements always stopped, and further observation never showed a recovery of clinical or bioelectrical activity of the brain.

To date, the mechanism and functional topography of the PATEO phenomenon with BSP remain undetermined. The lethality of this symptom is undisputed and has been confirmed in the cases presented. However, its ictal origin remains the main subject of discussion. Despite its small surface area, the upper eyelid has a complex neuromuscular apparatus and central innervation pathways. Two transverse striated muscles, the orbicularis oculi and the levator palpebrae (LP), are responsible for eyelid opening. The upper tarsal muscle, which is composed of smooth muscle tissue and is innervated by fibers from the upper cervical sympathetic node, adjoins the anterior surface of the LP. The motor neurons of the LP are located in the central parts of the caudate nucleus and are controlled by the premotor parts of the cerebral cortex, while the surrounding gray matter is involved in maintaining the tonic activity of this muscle [19].

The first publications describing PATEO suggested that this sign was a special type of postanoxic myoclonus with the location of the abnormal source of activity in the brainstem. Neurophysiological

Table 3. Neurophysiological characteristics of myoclonus depending on the anatomical localization of the source of abnormal activity.

Neurophysiological characteristics	Localization		
	Cortical	Subcortical	Segmental and peripheral
EEG	Epileptiform activity — generalized spike waves	No specific signs, may be totally absent	No specific signs, may be totally absent
Duration of muscle contraction	20–70 ms	75–300 ms	>100 ms
Inverse averaging of EEG by myogram	Characteristic activity 30-40 ms before muscle contraction	No activity	No activity

characteristics of myoclonus depending on the anatomical location of the source of abnormal activity are presented in Table 3, but all are characterized by a muscle contraction duration of less than 300 ms [20].

The presence of epileptiform impulses in the bursts, the long duration of the eye opening/closing phase, which significantly exceeds the duration of the myoclonus, indicates the failure of the hypothesis that PATEO with BSP represents subcortical myoclonus.

Electroencephalographic BSP reflects the functional dissociation of the brain, which can occur both under the influence of sedatives and in its diffuse damage [21].

Depending on the etiology of the disease, the predictive value of BSP may vary, but in anoxic injury it always indicates an unfavorable prognosis [22, 23]. The same morphology of bursts in BSP is a consistent ominous sign. The analysis of the EEG of 101 patients with BSP by Hofmeijer J. et al. showed that this particular type of bursts can only be observed in patients with diffuse cortical lesions, most often due to acute anoxia [24].

For the first time, we performed a software superimposition of bursts in BSP in patients with PATEO (Fig. 2), which showed their complete identity, including the morphology of muscle oscillations registered by the myographic channel. This finding supports the hypothesis that PATEO is a phenomenon of periodic disinhibition of nuclei located in the medulla oblongata due to acute extensive cortical and subcortical injury and is similar in origin to BSP with the same morphology of bursts. This is also supported by the obligatory occurrence of the sign in the acute phase of brain damage, its rapid exhaustion without recurrence, and its absolute fatality with any intensive care strategy. The only «less ominous» case of PATEO with BSP described in the literature [18] may have been a non-convulsive status epilepticus with minimal motor manifestations due to the underlying drug sedation.

The hypothesis of ictal origin of PATEO is based on the evaluation of the «epileptiform» morphology of the bursts and their relationship with the corresponding motor manifestations. In a number of patients presented in the literature review above [10, 14], PATEO had a different morphology and was also accompanied by epileptiform activity during which the eyes remained open. It is likely that the reported patients had a combination of PATEO and non-convulsive status epilepticus, which is common in patients after CPR [25]. Cases of similar tonic eye opening in response to painful nipple stimulation in patients who were declared brain dead further support our assumption of the non-ictal nature of PATEO [26].

Conclusion

The reported cases of the combination of BSP and periodic nonrhythmic tonic eyelid opening and the review of the literature indicate a very ominous character of this sign. The origin of PATEO remains controversial, but in our opinion it could be due to the disinhibition resulting from the cessation of control of dead cortical neurons over the nuclei of subcortical and stem structures, which still retain partial bioelectrical activity.

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