CASO CLÍNICO/CASE REPORT

Resolution of Epileptic Spasms After Drainage of Chronic Subdural Hematoma Related to Nonaccidental Traumatic Brain Injury

Resolução de Espasmos Epiléticos Após Drenagem de Hematoma Subdural Crónico Relacionado com Lesão Cerebral Traumática Não Acidental

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Abstract

Epileptic spasms (ES), an age-related seizure type, can occur due to a traumatic brain injury (TBI), after a seizure-free latency period. Its pathophysiological process is not fully understood. We report the case of a 5-month-old infant that presented an extensive encephalomalacia, right greater than left, and bilateral subdural hematomas secondary to nonaccidental TBI. Two months post-injury, the patient developed drug-resistant asymmetric ES, primarily involving the left limbs. The diagnosis was established based on electroclinical features. Subsequent brain magnetic resonance imaging (MRI) disclosed a progression of the left chronic subdural collection with associated mass effect. The subdural collection was drained, and resolution of ES was gradually observed after the procedure. This clinical report highlights the resolution of ES associated to nonaccidental TBI after drainage of a chronic subdural hematoma. The chronological association between these two events may provide some insight into the pathological mechanism underlying ES.

Resumo

Espasmos epiléticos (EE), um tipo de crise relacionada com a idade, podem ocorrer devido a lesão cerebral traumática (LCT), após um período de latência sem crises. A sua fisiopatologia não é totalmente compreendida. Relata-se o caso de uma criança de 5 meses que apresentava extensa encefalomalácia, maior à direita, e hematomas subdurais bilaterais secundários a LCT não acidental. Dois meses após a lesão, o doente desenvolveu EE assimétricos fármaco-resistentes, envolvendo principalmente os membros esquerdos. O diagnóstico foi estabelecido com base em características eletroclínicas. A ressonância magnética (RM) cerebral subsequente revelou progressão da coleção subdural crónica esquerda com efeito de massa associado. A coleção subdural foi drenada, verificando-se resolução gradual dos EE após o procedimento. Este caso clínico destaca a resolução de EE associados a LCT não acidental após a drenagem de um hematoma subdural crónico. A associação cronológica entre estes dois eventos pode ajudar a compreender o mecanismo patológico subjacente aos EE.

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Introduction

Epileptic spasms (ES) are characterized by a sudden, symmetric or asymmetric, flexion or extension of the axial and/or proximal limbs.[1] ES are often drug-resistant and continuous daily clusters invariably cause regression of developmental milestones.[2,3] Indeed, refractory ES are associated with epileptic encephalopathy and poor neurodevelopmental outcome.[2,3] Despite the development of various animal models,[4] the pathophysiology of ES remains unknown.

The etiology of ES is highly heterogeneous, including various genetic, metabolic, and structural causes.[2,3,5] Postnatal etiologies are less frequent than prenatal or perinatal etiologies.[5,6] ES can occur after a postnatal cerebral injury, as the first seizure type or following the onset of other seizures types.[7] Only a few reports on patients with ES associated with nonaccidental traumatic brain injury (TBI) have been reported (**Table 1**).[6-9] All cases suffered cerebral insults during early infancy and subdural hemorrhages were the most frequent type of

Table 1. Overview of previous reports on epileptic spasms after nonaccidental head trauma.

References	Sex	Age at injury (months)	Type of injury (neuroimaging)	Age at onset of ES (months)	Interval between injury and ES (months)	Hypsarrhythmia	Neurosurgical interventions? (type)	Outcome
Index patient	M	5	Brain CT: extensive, right, acute subdural hematoma, and diffuse cerebral edema. Brain MRI: extensive encephalomalacia, right greater than left. Bilateral subdural hematomas. Later, progression of the left chronic subdural collection with associated mass effect	7	2	No	Yes (emergent hinge craniotomy for acute subdural hematoma evacuation; VP shunt for hydrocephalus; burr-hole craniectomy with subdural drain placement for chronic subdural hematoma evacuation)	Severe developmental delay; left spastic hemiparesis.
Wang *et al* (2014)[8]	F	3	Brain CT: symmetrical subdural effusions in the bilateral frontotemporal areas. Brain MRI: subdural effusions in the supratentorium with a fluid-fluid level in the left parietal region.	3	-	No	Yes (craniostomy with drainage of hematomas)	-
Birca *et al* (2014)[9]	M	3	Brain MRI: multiple subdural hematomas, small areas of parenchymal contusions, and a subarachnoid hemorrhage.	6	3	Yes	No	Severe developmental delay, poor eye contact, mild spasticity.
	M	1	Brain MRI: multiple subdural hematomas, subarachnoid and intraventricular hemorrhage, occipital bone fracture, encephalomalacia in the left frontal and temporal regions.	5	4	Yes	No	Mild developmental delay.
Park and Chugani (2017)[7]	M	2	Brain CT: acute skull fracture. Brain MRI: chronic multicystic encephalomalacia.	-	24	No	No	Severe developmental delay, cortical blindness, spastic quadriplegic cerebral palsy.
	M	2,5	Brain CT: subdural hemorrhage, hydrocephalus.	-	7	No	Yes (VP and subdural shunts for hydrocephalus)	Cognitive delay, epileptic encephalopathy, left hemiparesis.
Takeda *et al* (2020)[6]	M	5	Brain CT: acute left subdural hematoma and a posterior, interhemispheric subdural hematoma with subjacent hemispheric swelling and a midline shift Brain MRI: cerebral atrophy and ventriculomegaly, predominantly in the left hemisphere.	10	5	Yes	Yes (emergent surgery to remove the acute subdural hematoma)	Severe developmental delay, predominant right-side spastic quadriparesis.
	F	4-5	Brain CT: bilateral frontal hypointensity without any skull fracture. Brain MRI: parenchymal clefts in the subcortical white matter of the frontal lobes (contusional tears).	6	1-2	Yes	No	Moderate development delay.

ES: epileptic spasms; M: male: F: female; CT: computed tomography; MRI: magnetic resonance imaging; VP: ventriculoperitoneal

brain injury.[6-9] ES occurred mainly after a latency period ranging from 2 months to 2 years after a head trauma.[6,7,9]

We report an infant's case, whose drug-resistant ES stopped after evacuating a chronic subdural hematoma related to a past nonaccidental TBI. The chronological association between these two events may provide some insight into the pathological mechanism underlying ES development.

Case Report

A previously healthy 5-month-old boy, born at full-term after an uncomplicated pregnancy and delivery, was admitted to an emergency department. He presented altered mental status and prolonged convulsive seizure with apnea that responded to cardiopulmonary resuscitation. Information about the nature and duration of the cardiopulmonary resuscitation was not available. Levetiracetam 40 mg/kg/day was started, without seizure recurrence. Besides the altered mental status, further examination revealed a left retinal hemorrhage. Brain computed tomography (CT) showed an extensive, right, acute subdural hematoma, and diffuse cerebral edema, in the absence of skull fracture. An emergent hinge craniotomy for subdural evacuation was performed. A skeletal survey, metabolic and infectious work-ups were unremarkable. Based on the clinical and neuroimaging findings, the diagnosis of non-accidental brain injury was established with the perpetrator's subsequent identification.

During hospitalization, neurological examination revealed an absent response to visual stimuli, a decreased truncal tone, and left hypertonic hemiparesis. The patient's brain magnetic resonance imaging (MRI), 20 days after presentation, showed extensive ischemia of the right hemisphere and bilateral extra-axial hemorrhages, more prominent in the right cerebral convexity (**Fig. 1A**). On day 22 post-TBI, a left-sided ventriculoperitoneal shunt was placed to treat the post-traumatic hydrocephalus. There were no complications associated to the neurosurgical procedure. The patient presented *de novo* right arm clonic seizures, correlated with an ictal electroencephalogram (EEG) pattern involving the left temporo-parietal area. The seizures were easily controlled with an increased maintenance dose of levetiracetam (60 mg/kg/day). Interictal EEG demonstrated: generalized continuous slowing of brain waves; abundant epileptiform discharges in the left hemisphere, with varying maximum negativity; and in the right hemisphere, epileptiform discharges mainly in the frontal head region, with attenuation of brain wave activity in the posterior head region. A follow-up neuroimaging showed a marked bi-hemispheric cystic encephalomalacia, right greater than left. Both bilateral extra-axial collections remained stable over time and with no significant mass effect.

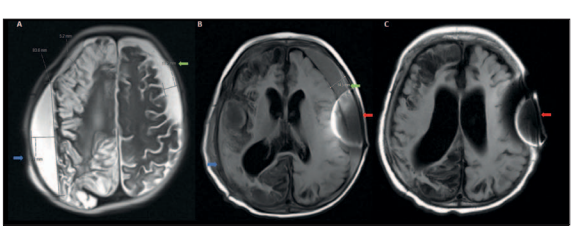

Figure 1. Brain MRI.

A) Axial T2W – Twenty days post-TBI. Postoperative changes of right lateral hinge craniotomy. Extensive encephalomalacia of right cerebral hemisphere. Bilateral extra-axial hemorrhage: 19.2 mm transverse diameter in the right hemispheric convexity (blue arrow) and 11.2 mm in the left frontoparietal region (green arrow).
B) Axial FLAIR – Two months post-TBI. Left shunt valve artifact (red arrow). Evolution with ex-vacuo ventriculomegaly, regression of the right subdural fluid collection (blue arrow). Note an increased size and posterior extension of the left hemispheric collection with 14.5 mm transverse diameter (green arrow).
C) Axial FLAIR – Nine months post-TBI and 5 months after drainage of the left subdural collection. Extensive bilateral encephalomalacia. No subdural collections. Left shunt valve artifact (red arrow).

The patient was clinically stable and seizure-free for seven weeks until abundant clusters of asymmetric ES began at 7 months of age. The clusters occurred 5-7 times daily, invariably after sleep/nap, for 1-5 minutes per cluster. Each spasm primarily involved the left limbs, and included an abrupt, incomplete internal rotation and extension of the left arm with left leg's extension associated with eye deviation to the left. In a cluster, each spasm lasted ~2.6 seconds and occurred every other second. Spontaneous movements of all 4 limbs alternated with each spasm (Video supplement). The ictal EEG was characterized by repetitive, high amplitude (~300-400 μV on reference montage with electrically silent A2 reference), irregular slow waves (~2Hz) on the left hemisphere and right frontal head region, associated with each spasm, alternating with a brief period of voltage attenuation (~2 seconds) (**Fig. 2A**). The ES were refractory to an increased levetiracetam dose (80 mg/kg/day), in combination with vigabatrin (150 mg/kg/day) and clobazam (0.7 mg/kg/day). After 40 days on a stable vigabatrin dose, a ketogenic diet was started and maintained for three months, also without any therapeutic benefit. Throughout this time, his shunt setting was slowly increased to reduce the drainage. A control brain MRI showed encephalomalacia with ex-vacuo ventriculomegaly and regression of the right subdural collection. However, a posterior extension of the left subdural collection was now associated with mass effect and signal evolution to chronic hemorrhage (**Fig. 1B**). Due to the slowly increasing size of the left subdural hematoma a decision was made to evacuate it. There were neither changes in the antiepileptic drug regimen

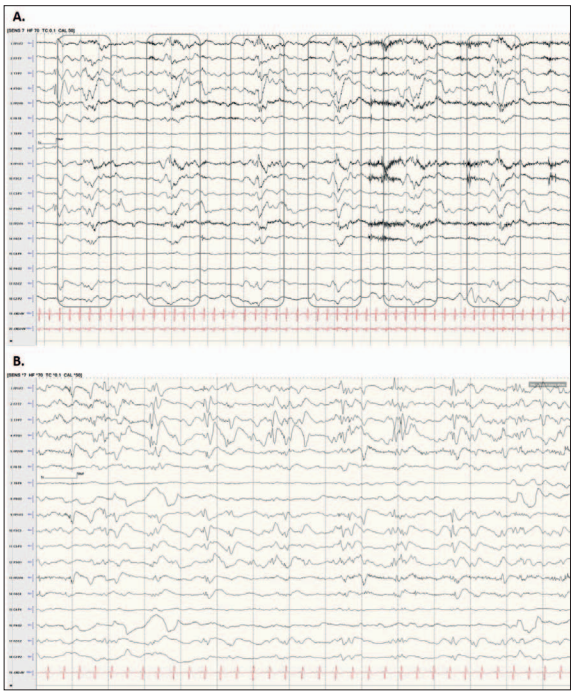

Figure 2. Electroencephalogram (Bipolar montage; Sensitivity 7 µV; High frequency 70 Hz; Time Constant 0.1 sec)

A) 24 hours prior to left chronic subdural hematoma evacuation – Epileptic spasms occurring every ~1 second in a cluster during a 30 seconds of EEG recording. Grey box indicates EEG changes associated with spasms.
B) 14 months post-TBI and 10 months after left chronic subdural hematoma evacuation. Sharp waves in the left hemisphere with varying maximum negativity during 15 seconds of EEG recording.

nor in the frequency of ES for at least one month before the surgery. The patient underwent a burr-hole craniectomy with subdural drain placement, and the left subdural fluid collection was evacuated without any complication. The temporary subdural drain was removed on post-operative day two. Immediately after surgery, ES began to gradually space out in frequency and shortened in duration until they stopped on post-operative day 18. Spasms resolution was confirmed clinically and on continuous video-EEG monitoring. Ketogenic diet and vigabatrin were, therefore, slowly weaned off, maintaining the remaining antiepileptic drugs. Posteriorly, clobazam was also tapered until suspension.

An MRI obtained five months following subdural hematoma evacuation demonstrated no recurrence (**Fig.1C**). A follow-up video-EEG at 19 months of age disclosed epileptiform discharges in the left and right hemisphere similar to those reported before the surgery. No seizures were recorded (**Fig. 2B**). The patient continued to be seizure-free, at that time only with levetiracetam 60 mg/kg/day. The parents reported subjective progression of vocalization and spontaneous limb movements, especially during their son's interaction. The neurologic examination revealed a severe developmental delay with profound post-traumatic neurologic sequelae, including left spastic hemiparesis.

Discussion

Post-traumatic epilepsy occurs in 10%-20% of children following severe TBI; however, the incidence of epileptic spasms after a TBI is unknown.[10] According to previous studies, the estimated risk of developing post-traumatic ES is 1.8%, and it is higher if TBI occurs in early infancy compared to childhood.[7]

In the index patient, the diagnosis of ES was made based on seizure semiology. The neurophysiological features supported this diagnosis instead of tonic seizures. The clinical features were brief (<3 seconds) and repetitive clusters of spasms that were often associated with awakenings. Kellaway *et al* reported, using muscle tracings, that the initial contraction phase in an ES lasted less than two seconds, which was followed by a sustained contraction lasting 2-10 seconds.[1] Our patient's abrupt initial contraction of primarily left limbs, followed by a brief sustained tonic phase, lasted a total of ~2.6 seconds. In contrast, tonic seizures usually last at least three seconds.[11] Differentiating tonic seizures of Lennox Gastaut Syndrome (LGS) from ES may be difficult sometimes. However, the occurrence of these type of seizures and the corresponding diagnosis are commonly age-dependent. LGS may be an evolution of clinical and neurophysiologic characteristics of West syndrome.[12] The diagnosis of LGS is typically apparent by the age of 3 years, and ES usually occur in children between 3 months to 12 months.[12] ES in our patient began at 7 months of age, 2 months after TBI.

The associated ictal EEG of the index patient was characterized by irregular high amplitude slow waves in the left hemisphere and right frontal head region, alternating with a brief period of voltage attenuation. This ictal EEG is corroborated by the commonly described ictal EEG pattern associated with ES – generalized high amplitude, irregular slow waves followed by a voltage attenuation of fast frequency waves with a positive phase reversal over the vertex region.[13] The "absence" of background rhythm in the right posterior head region is most likely due to the severe encephalomalacia.

Hypsarrhythmia, considered an interictal EEG finding, is typically associated with ES.[2] It is observed in 40%-70% of patients with ES.[12] Hypsarrhythmia was absent in the index patient, which may be related to the severe global TBI with much of the right hemisphere presenting encephalomalacia. Indeed, children with severe lesional encephalopathies may lack hypsarrhythmia.[7,14,15]

The pathophysiology of how epileptic spasms develop after a cerebral insult is unknown. A possible scenario

could be that of a disruption of the normal brain neuronal/interneuronal networks, leading to abnormal interactions between cortex, subcortical structures, and brainstem at a critical maturation stage.[2,7] In our patient, the timing effect of left subdural fluid evacuation and subsequent resolution of ES after the procedure, without prior changes to the medication regimen, suggests an association between these two factors. Even though both hemispheres were injured, the right hemisphere suffered a more significant injury, as indicated by left hypertonic hemiparesis, MRI findings and decreased EEG background rhythm in the right posterior head region. Thus, ES may have arisen from the right hemisphere. After the review of 75 consecutive video-EEG recordings of infantile spasms (8680 spasms), Gaily *et al* noted that most asymmetric or asynchronous spasms were associated with an ictal EEG discharge that was contralateral to the more symptomatic side during spasms.[16] Baseline EEG, radiologic studies (brain MRI, PET), and neurological examination revealed structural and functional brain abnormalities that involved the contralateral central region significantly more often in the children with >50% spasm asymmetry or asynchrony.[16] The reason why the left chronic subdural hematoma evacuation resulted in the resolution of ES, which likely arose from the right hemisphere, remains elusive. Nevertheless, the mass effect secondary to a subdural collection, in the setting of a maturing brain, may play a role in the development of ES after head trauma. The cessation of ES after the relief of intracranial pressure by neurosurgical treatment supports this hypothesis.

Infants with epileptic spasms, unlike other seizure types, are especially challenging to treat due to a limited number of antiepileptic drugs showing therapeutic benefit.[2] Untreated infants invariably regress developmentally and become encephalopathic.[2,14] TBI is an important risk factor for postnatal epileptic spasms.[6,7,9] In these cases, a neurosurgical intervention may be an option (**Table 1**).[6-8] In the index case, epileptic spasms stopped after drainage of a subdural fluid collection related to a diffuse nonaccidental TBI. This association could add some insight into the pathological mechanism of ES development. ■

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