

Apneic Seizures: A Sign of Temporal Lobe Hemorrhage in Full-Term Neonates

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Intracranial hemorrhage is a common cause of neonatal seizures in full-term infants. However, only some infants with intracranial hemorrhage come to clinical attention. A right temporal lobe hemorrhage with resulting apneic seizures was described previously in one neonate. In this case report, we review three full-term male neonates with no significant perinatal complications who presented with apneic events and temporal lobe hemorrhage. One neonate had apnea as the sole manifestation of a seizure that was confirmed electrographically. One neonate had motor manifestations of seizures, in addition to apnea, that were confirmed as seizures electrographically. The third neonate had pure apneic events before initiation of electroencephalogram monitoring which were presumed to be seizures, because the electroencephalogram demonstrated epileptiform abnormalities. At follow-up, all three children were neurodevelopmentally normal. This case report emphasizes that, although uncommon, full-term neonates may present with apnea as the initial manifestation of temporal lobe hemorrhage. Because apnea could be a manifestation of a seizure, continuous electroencephalogram monitoring should be considered in a full-term neonate with unexplained apnea. © 2007 by Elsevier Inc. All rights reserved.

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Introduction

Intracranial hemorrhage is the cause of neonatal seizures in 17% of full-term infants, and is more commonly seen after vaginal delivery assisted with forceps or vacuum extraction. However, only some infants with intracranial hemorrhage come to clinical attention [1]. The etiology of intracranial hemorrhage, its extent, and the compartments involved determine the clinical presentation and outcome.

Apnea in a newborn can result from various causes. Apnea is described as cessation of breathing for >15 seconds. Underlying causes include prematurity, sepsis, gastroesophageal reflux, pulmonary disease, arrhythmias, and intracranial hemorrhage, among others. Apnea can also be the only manifestation of a seizure.

The association of temporal lobe intracranial hemorrhage and apneic seizures in full-term neonates was reported previously [3]. The previous literature and our three case presentations demonstrate the need for an index of suspicion for seizures as the etiology of apnea, and a need to initiate continuous electroencephalogram monitoring in neonates with unexplained apnea.

Case Report

We describe three neonates who presented with apnea as the initial manifestation of underlying temporal lobe hemorrhage. The pregnancy and perinatal histories of the three neonates are summarized in Table 1.

All three neonates had sepsis evaluations at presentation, and were started on antibiotics pending cultures. Initial laboratory test results, including hematocrit, platelets, and chemistries (electrolytes, glucose, calcium), were normal.

An electroencephalogram was performed using digital equipment from XLTEK (Oakville, Ontario, Canada), with a standard neonatal montage in all patients. The main clinical, electrographic, and imaging findings, hematology investigations, cardiology evaluations, and clinical follow-up information from the three neonates are summarized in Table 2.

Patient 1

With his first feed 3 hours after birth, this male neonate was noted to be dusky, and was transferred to our Neonatal Intensive Care Unit. Subsequently, he had recurrent periods of apnea for 20-50 seconds, with oxygen desaturations to 50 percent during periods of apnea. One episode was associated with conjugate eye deviation to the right, and right-arm clonic jerking, lasting 30 seconds. No changes in heart rate were observed during these events.

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Patient	GA (wk)	Sex	BW (g)	Apgar Scores (1 min/5 min)	Complications of Pregnancy, Labor, and Delivery
1	40	М	3300	9/9	None, NSVD
2	39	М	3545	9/9	PROM > 20 hr, NSVD
3	37	Μ	3660	7/9	None, NSVD
Abbreviations:					

BW = Birth weight

GA = Gestational age

M = Male

NSVD = Normal spontaneous vaginal delivery

PROM = Premature rupture of membranes

An examination showed a head circumference of 33.5 cm (10th percentile for age). His vital signs were normal. No cephalhematoma was noted. He had a gaze preference to the left (likely a postictal state) that resolved over the next 24 hours. A neurologic examination produced normal results otherwise. Lumbar puncture results were significant for 53,000 red blood cells.

Electroencephalogram monitoring demonstrated multiple electrographic seizures of left hemispheric origin that were clinically accompanied by apnea and oxygen desaturation. The onset of apnea was 5 seconds after the onset of electrographic seizure.

The patient was intubated for recurrent apnea, and was concurrently loaded with phenobarbital. Apneic events and electrographic seizure activity resolved after a phenobarbital level of 34 μ g/mL was attained.

A head ultrasound demonstrated an echogenic focus in the left temporoparietal area. Magnetic resonance imaging indicated a left temporal and parietal intraparenchymal hemorrhage, with adjacent subdural hematomas. Magnetic Resonance Angiogram and Magnetic Resonance Venogram produced normal results.

Figure 1 depicts a characteristic electrographic seizure emanating predominantly from the left temporal lobe which was accompanied clinically by apnea and oxygen desaturation. Seizure was characterized at onset by sharply contoured, rhythmic delta activity for 3-5 seconds. This activity evolved into faster-frequency alpha with admixed theta sharpand slow-wave activity, most prominent in the left temporal region. This activity lasted 25 seconds, and was followed by diffuse attenuation and slowing. Figure 2 is an axial, gradient echo sequence demonstrating a left temporal lobe hemorrhage with an adjacent subdural hematoma.

Subsequent magnetic resonance imaging of the brain at age 10 days revealed restricted diffusion of the left temporal cortex suggesting infarction, the expected evolution of subdural hematomas, and a resolution of the minimal mass effect.

An electroencephalogram at age 12 days indicated frequent left temporal spikes at T3 and T5, with phase reversal at T3 accompanied by no behavioral change. No seizures were noted. Continuous left hemispheric attenuation occurred.

Patient 2

At 2 hours of age, this newborn male had apneic episodes with oxygen desaturations to 40 percent. There was no relationship of these episodes to feedings. No change in heart rate was observed during the episodes. No movements suggesting seizures were noted. During these events, he responded to vigorous stimulation and blow-by oxygen.

His examination showed a head circumference of 36 cm (90th percentile for age). His vital signs were normal. There was no cephalhematoma or skull fracture. No neurologic deficits were found. A head ultrasound obtained at age 2 days indicated echogenicity in the posterior right temporal lobe. Magnetic resonance imaging revealed a right temporal intraparenchymal hemorrhage, and Magnetic Resonance Venogram demonstrated a right sigmoid sinus thrombosis. Hypercoagu-

lability laboratory tests and a cardiac workup for the etiology of the sinus thrombosis were unrevealing.

He did not have any apneic events after the initiation of continuous electroencephalogram monitoring. Abnormal electroencephalogram findings included focal slowing and epileptiform features on the side of the hemorrhage. The etiology of apnea was presumed to be seizures, but this could not be confirmed, because the last documented apneic event was before initiation of the electroencephalogram. Because he did not have any further events, he was not started on antiepileptic medication.

Patient 3

At 2 minutes of life, this male neonate required intermittent positive pressure ventilations for a dusky appearance. At about age 5 hours, he had episodes of dusky appearance and desaturation to 30 percent followed by apneic events requiring positive pressure ventilations.

Examination indicated an infant who was large for his gestational age. His vital signs were normal. A neurologic examination produced normal results. During his first day of life, several further episodes of brief apnea and desaturations occurred, which were unrelated to feedings and did not respond to antireflux measures.

At day 1 of age, a computed tomography scan revealed a small hemorrhage in the right temporal lobe, with no mass effect. Magnetic resonance imaging confirmed a right temporal lobe hemorrhagic infarct. Magnetic Resonance Angiogram yielded normal results.

Continuous electroencephalogram monitoring captured a 90-second apneic event with no associated bradycardia. This was associated electrographically with right temporal lobe rhythmic spike and wave activity. The infant was started on phenobarbital with no further events. An electroencephalogram at age 6 days and at 3 months showed occasional right central and temporal sharp waves, but no ictal sequences were recorded.

Phenobarbital was gradually withdrawn at age 6 months. He was seizure-free until age 4 years, when he had complex partial and secondary generalized seizures. Carbamazepine was initiated, with good seizure control.

Discussion

Apnea as sole manifestation of a seizure in a full-term neonate is rare [3]. One report described four term neonates with apnea and additional motor movements correlating with electrographic seizures [4]. Watanabe et al. [2] described 19 term neonates with apnea and electrographic seizures, of whom only three were purely apneic, and 11 had an associated, subtle clinical phenomenon. One of the four term neonates with apnea and

Table 2. Clinical features, investigations, and follow-up information

		Patient	
	1	2	3
Age at presentation	3 hr	2 hr	5 hr
Clinical history	Apnea Eye deviation to right Right-arm clonic movements	Apnea	Apnea
Ictal electroencephalogram activity	Four seizures: LH onset, 5-6-Hz spike and wave activity, with phase reversals at T3 associated clinically with apnea	None	RT rhythmic spike and wave activity with apneic events
Duration of seizures (seconds)	120-180	N/A	90
Interictal electroencephalogram activity	Frequent LH spike and wave activity at Fp1, C3, T3 Rare independent RH sharp waves at FP2 and T4	Bursts of RH high-voltage delta Multifocal sharp waves Bursts of RH occipital theta	Right-sided slowing
Antiepileptic drug therapy	Phenobarbital	None	Phenobarbital Carbamazepine
Imaging	LTP intraparenchymal and LT SAH Bilateral infra/supratentorial	RT intraparenchymal hemorrhage with restricted diffusion Right tentorial subdural hematoma	RT edema and hemorrhagic infarct underlying right sylvian fissure SAH
MRA/MRV	Normal MRV findings Normal MRA findings	MRV: right sigmoid sinus thrombosis Normal MRA findings	Normal MRA findings
Follow-up magnetic resonance imaging	5 months later Encephalomalacia in LT lobe, resolved subdural hematomas	3 months Encephalomalacia in RT lobe Recanalization in right sigmoid sinus	
Hematology workup for etiology	Unrevealing	Unrevealing	Unrevealing
Cardiology workup	Negative	Negative	
Seizure-free	Yes	Yes	No
Follow-up (months)	5	11	84
Neurodevelopment	Normal, possible left-hand preference	Normal	Normal
Abbreviations: LH = Left hemispheric LT = Left temporal LTP = Left temporarietal MRA = Magnetic resonance angi MRV = Magnetic resonance vene N/A = Not available RH = Right hemispheric RT = Right temporal SAH = Subarachnoid hemorrhag	iogram ogram ge		

electrographic seizures described by Monod et al. [5] had pure apneic seizures. Tramonte and Goodkin [3] reported a full-term neonate with apnea as the presenting symptom of temporal lobe hemorrhage.

Apnea occurring beyond the neonatal period is very rare, and has received attention as a possible precursor to apparent life-threatening events [7]. Previous reports found that intracranial hemorrhages in the majority of infants with apneic seizures are in areas other than the temporal lobes [6]. Although the neonates we describe had hemorrhages predominantly in the temporal lobes, this may be because of the small number of patients in our study.

Epileptic apnea is thought to originate from the limbic system [2,7]. Electroencephalograms in older infants and children with apneic seizures usually indicate focal repetitive spike and wave discharges, most often originating in the temporal lobes without a corresponding structural lesion [6,7]. In contrast, the ictal electroencephalograms of apneic seizures of most previously reported newborns demonstrate bilateral rhyth-



Figure 1. Shows Patient 1, EEG: Seizure of Left hemispheric onset.

mic monomorphic activity in the theta and alpha bands, originating in the central areas [8].

Our patients were unusual, in that 2 of 3 neonates had temporal lobe ictal and interictal epileptiform activity, similar to the electroencephalogram findings in older infants with apneic seizures, and differing from most reported neonates with apneic seizures who have more generalized abnormalities. In addition, unlike older infants, our patients had structural abnormalities corresponding to the ictal focus described in one previous neonate [3].

The background activity of the electroencephalogram was normal for age, which correlated with their good short-term developmental outcome. However, further follow-up is necessary to determine a long-term prognosis.

Intraparenchymal hemorrhage in the term infant is relatively uncommon [9]. Most neonates with isolated intraparenchymal hemorrhages are of normal birth weight, without prenatal complications, and with uncomplicated deliveries [10]. No specific cause for the bleeding is identified in many of these children [9,11]. Undetected hypoxic-ischemic injury was hypothesized to be a cause of intracranial hemorrhage in the term neonate. However, the high Apgar scores and eventual good outcome argue against this possibility [10].

Although all three neonates also had other compartments involved, the most significant abnormality in each was in the temporal lobe. This finding likely explains the favorable outcome.

Potential explanations for intraparenchymal hemorrhages include arterial and venous occlusion with hemorrhagic infarction. This occlusion may be secondary to emboli arising spontaneously from thrombosis in involuting umbilical veins, arteries, or the ductus arteriosus. Local trauma with resultant venous or capillary injury, and cortical trauma from parturition, are also implicated [9-12].

The sites of intraparenchymal hemorrhage in these reports were most commonly temporal. An unprotected sutural confluence adjacent to the pterion is postulated as



Figure 2. Shows Patient 1; MRI, Axial, Gradient echo sequence demonstrating Left Temporal parietal intraparenchymal & subarachnoid hemorrhage. (TR/TE = 400/15 ms, Flip angle; 20, Matrix; 256/192).

a potential location for vascular injury because of molding during delivery [13]. As in our three patients, surgical evacuation has not played a role in the management of the majority of infants described in the literature [12].

Conclusions

It is important to recognize that, although uncommon, full-term neonates may present with apnea as the initial manifestation of either right or left temporal lobe intracranial hemorrhage. Determination of the cause of apnea is important for proper treatment, because therapy differs according to diagnosis. A high index of suspicion should be maintained for seizures as the etiology of apnea. Continuous electroencephalogram monitoring is valuable in correlating apnea to electrographic activity, and should be considered in term neonates with unexplained apnea. Early detection of seizures can lead to investigation into the etiology and appropriate management of the intracranial hemorrhage and facilitate prompt management of seizures, which may help reduce the degree of neurodevelopmental disability.

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