

Asynchronous pentobarbital-induced burst suppression with corpus callosum hemorrhage

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Abstract

Objective: We describe the electroencephalographic (EEG) findings in a 9-year-old girl, who presented with generalized tonic-clonic status epilepticus requiring pentobarbital anesthesia, and correlate these findings with clinicoradiologic evidence of a ruptured AVM with hemorrhage into the body of the corpus callosum.

Methods: EEG analysis accompanied by clinical assessment, CT and MRI scans, and cerebral angiography were performed.

Results: With pentobarbital coma, the EEG showed burst suppression with prominent interhemispheric asynchrony. Suppression epochs >2 s in duration and with amplitude <20 μ V in all channels were identified. In 12 min of the EEG analyzed, 6 unilateral and 20 bilateral epochs occurred. Of the 20 bilateral suppression epochs, interhemispheric asynchrony of >1 s was noted at onset for 5 epochs and at offset for one. Chi-square analysis revealed an equal tendency for unilateral suppressions to occur over either hemisphere, and for suppression in one hemisphere to begin before the other.

Conclusions: We conclude that the corpus callosum plays a critical role in interhemispheric synchronization of cortical neuronal electrical activity and propose that: (1) normally, the corpus callosum modulates interhemispheric synchronization of cortical inhibition; and (2) with corpus callosal disruption, cortical areas are 'released' from such synchronization. © 1999 Elsevier Science Ireland Ltd. All rights reserved.

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1. Introduction

As increasing doses of barbiturates are given, the EEG shows an orderly progression of changes: increased fast activity, attenuation of the background amplitude, greater activity in the theta and delta frequency ranges, burst suppression, and finally complete suppression of all EEG activity.

The burst portion of a burst suppression pattern is generally defined as a bilateral, high amplitude, synchronous, and diffuse 'paroxysm' of activity of delta and theta frequencies. Sharp waves and spikes are usually present. As its name implies, the suppression period (also known as the interburst interval) electroencephalographically consists of absent or severely attenuated activity of delta and theta frequency (Chatrian, 1990). In diseases diffusely affecting cerebral cortical function, the bursts are bilaterally synchronous and the degree of attenuation during the suppression symmetrical.

Whether the burst suppression pattern occurs as a result of hypoxia, ischemia, encephalitis, or administration of anesthetic agents, deafferentation of the cortex from thalamic projections is thought to be the underlying pathophysiologic explanation (Fisch, 1991). Barbiturates, then, may effectively disconnect the cortex from the subcortical regions.

Pharmacologically-induced asynchronous interhemispheric burst suppression has not been reported. Spontaneously occurring asynchronous burst suppression has been noted with Aicardi's syndrome, a condition of female infants characterized by the clinical triad of chorioretinal lacunae, infantile spasms, and partial or complete agenesis of the corpus callosum (Fariello et al., 1977; Ohtsuka et al., 1993). Brenner and Schaul (1990) conclude that 'relatively little is known regarding the mechanism of periodic EEG discharges' but concede that a 'mechanism of synchrony and timing' must exist. Our report suggests that the corpus callosum provides such a mechanism.

1.1. Case report

A 9-year-old, left-handed girl presented with generalized tonic-clonic status epilepticus upon rupture of an AVM. CT

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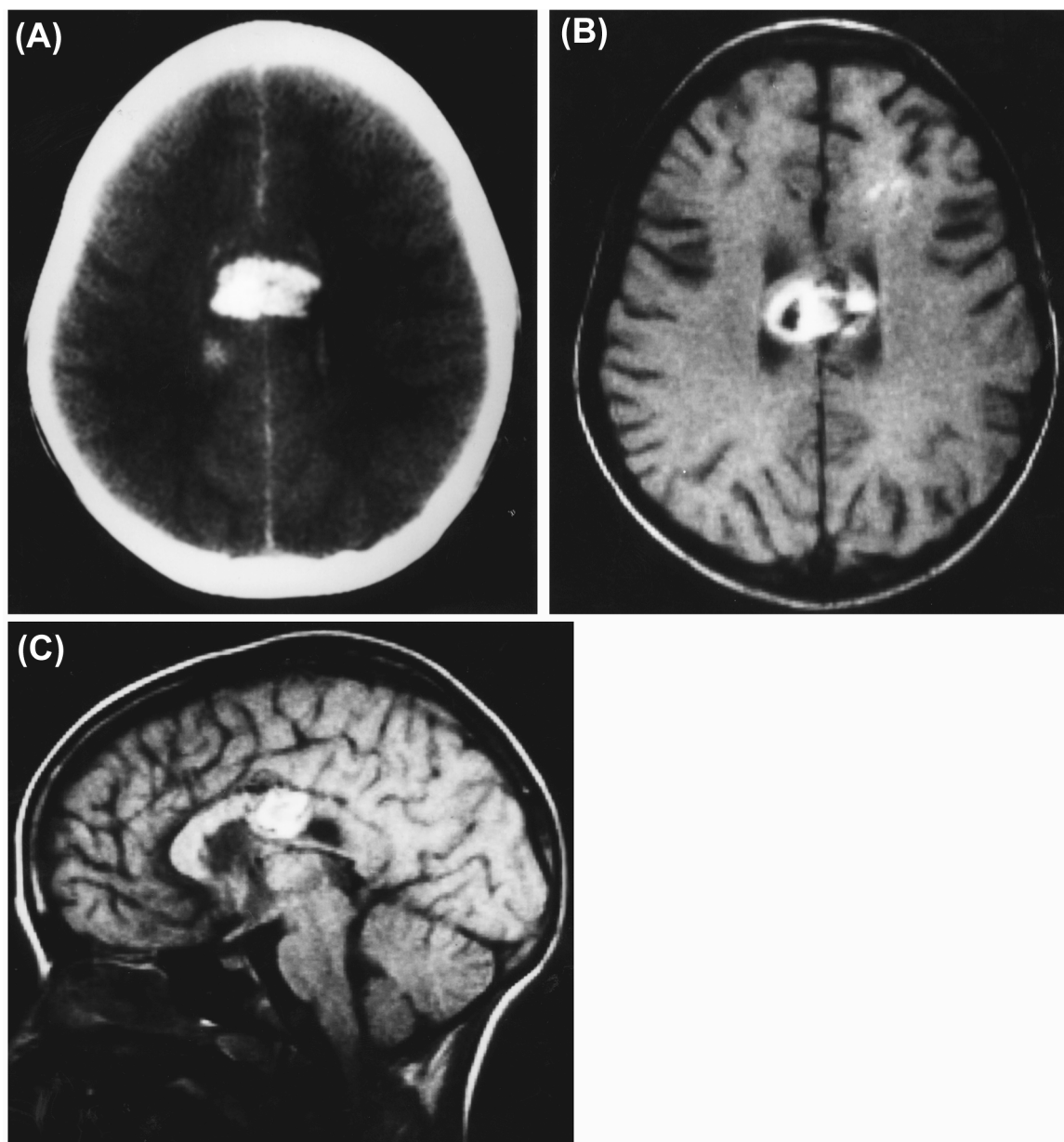


Fig. 1. (A) Transverse view of head CT scan performed on hospital admission demonstrates a 3 cm hematoma in the body of the corpus callosum. Intraventricular hemorrhage is also seen. Additional axial sections (not shown) revealed hydrocephalus with dilatation of the lateral ventricles and its temporal horns. (B) Axial view of T1 weighted MRI scan of the brain obtained on hospital day 18, demonstrates a large residual hemorrhage of mixed signal intensity in the corpus callosum. The punctate hyperintensities seen in the left frontal region (and in right frontal white matter, left basal ganglia, and right thalamus which are not shown) are attributed to ventriculostomy catheter placements. (C) Sagittal view of T1 weighted MRI scan of the brain obtained on hospital day 18, demonstrates the anatomical localization of the hemorrhage in the body of the corpus callosum.

and MRI scans revealed a 3 cm hematoma in the body of the corpus callosum, extensive intraventricular hemorrhage, and hydrocephalus (Fig. 1). Administration of mannitol, hyperventilation, left ventriculostomy catheter placement, and pentobarbital coma were instituted. Cerebral angiography revealed a 3×1.5 cm AVM involving the left pericallosal artery (Fig. 2).

Intermittently, increased intracranial pressure occurred requiring repositioning of the ventriculostomy catheter in

alternate hemispheres. Pentobarbital coma was discontinued on hospital day 9. Seizures did not recur.

After 1 week of mutism, the patient recovered language function but exhibited a mild left hemiparesis, left upper extremity dysmetria, and decreased short-term memory. Neuropsychological testing 7 months later indicated normal callosal transfer of tactile information as measured by the ability, with eyes closed, to choose by hand the same object simultaneously palpated by the other hand.

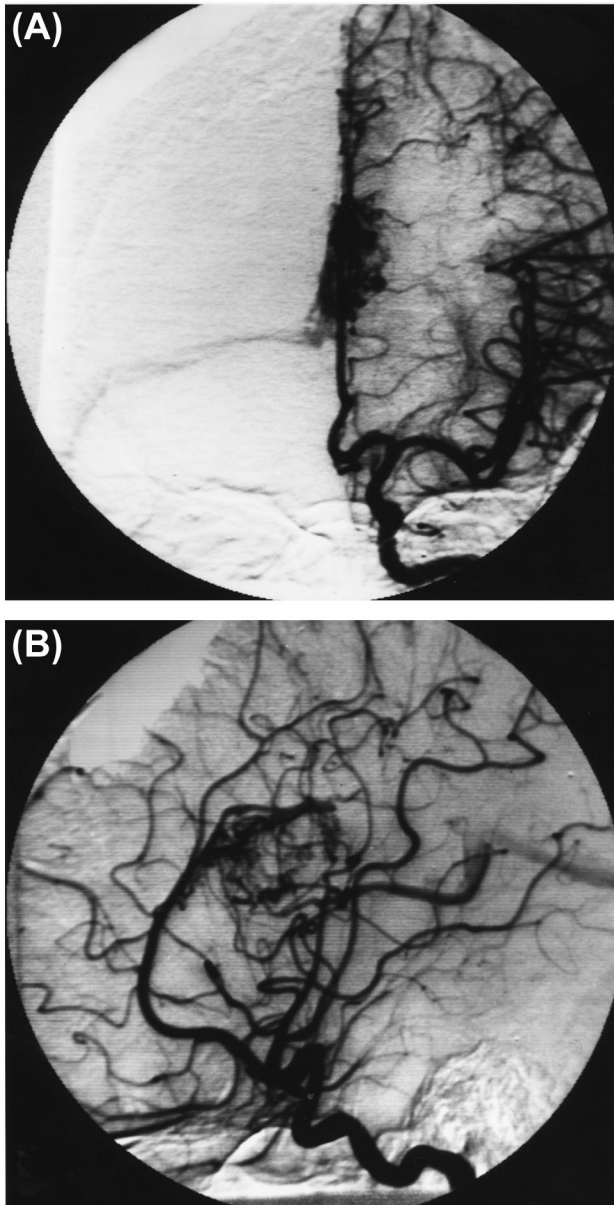


Fig. 2. (A) Rapid sequence digital AP cerebral angiogram reveals an AVM within the body of the corpus callosum supplied via the left pericallosal artery. (B) Lateral view of cerebral angiogram demonstrates a relatively hypovascular region in the central aspect of the AVM which may correspond to the hematoma noted in Fig. 1. The AVM measures 3×1.5 cm.

EEGs were recorded 2 days, 1 week, 1 month and 10 months after initial clinical presentation.

2. Materials and methods

EEGs were recorded with silver cup electrodes in longitudinal and transverse bipolar montages employing the International 10–20 system of electrode placement. A longitudinal bipolar montage was used for quantitative measurements.

Suppression epochs were defined as those periods with duration >2 s and amplitude $<20 \mu\text{V}$, in all channels of a given hemisphere. Both visual and statistical (Chi-square) analyses of the EEG were performed.

3. Results

Portions of the patient's initial EEG performed on hospital day 2 are shown in Fig. 3. Burst suppression with prominent interhemispheric asynchrony is evident. This EEG was performed prior to repositioning of the ventriculostomy catheter into the right hemisphere. The patient's serum level of pentobarbital at this time was 34.3 mg/l.

Visual analysis of 12 min of the initial EEG revealed 26 suppression epochs, with 6 occurring unilaterally and 20 occurring bilaterally. Of the 20 bilateral suppression epochs, interhemispheric asynchrony of >1 s was noted at onset for 5 of the epochs and at offset for 1. Chi-square analysis revealed an equal tendency for unilateral suppressions to occur over either hemisphere as well as for suppression in one hemisphere to begin before the other. Suppression epochs which met the above duration and amplitude criteria in all but one channel, commonly demonstrated persistence of activity in the frontopolar regions.

A repeat EEG performed 1 week following initial presentation continued to reveal burst suppression, but now with less prominent asynchrony. Serum levels of pentobarbital and phenobarbital at this time were 11.7 mg/l and 24.2 mg/l, respectively.

At 1 month follow-up, the EEG was normal in the awake and drowsy states (Fig. 4). At 10 months follow-up, an EEG performed in the sleep state revealed synchronous and symmetric sleep spindles.

4. Discussion

Our patient's clinical presentation with mutism and leg weakness coincides with descriptions of behavior following anterior corpus callosum section for intractable seizures (Roberts, 1991). The anatomic basis for such mutism has been attributed to a 'disconnection' of white matter tracts which originate in the anterior cingulate and supplementary motor areas of the frontal lobe and traverse the body of the corpus callosum (the location of the lesion in our patient) (Pandya and Rosene, 1985).

Roles for the corpus callosum in interhemispheric integration and synchronization of neuropsychological and neurophysiological processes follows from analyses of EEG abnormalities which accompany callosal disruption. For example, asynchrony of EEG sleep spindles and decreased coherence at frequencies less than 4 Hz have been noted in patients with callosal agenesis (Lynn et al., 1980; Kuks et al., 1987). Following total corpus callosum section, desynchronization of the ictal onset of bilateral hemispheric discharges is electrographically seen (Spencer



Fig. 3. EEG performed on hospital day 2 showing burst suppression with prominent interhemispheric asynchrony. Occasional multifocal sharp wave discharges are noted within the asynchronous and synchronous bursts.

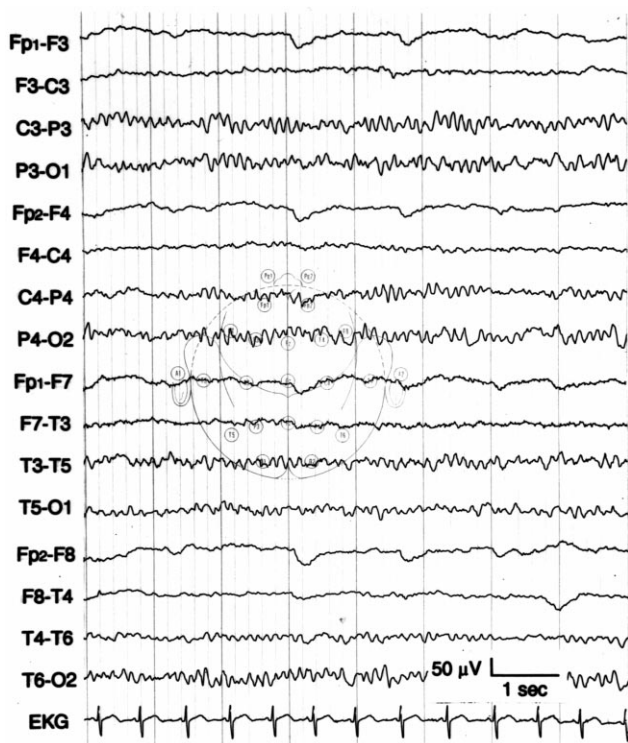


Fig. 4. Normalization of EEG performed 1 month following clinical presentation.

et al., 1993) supporting a role for the corpus callosum in the secondary generalization or synchronization of epileptic activity.

The persistence of bilaterally synchronous interictal EEG discharges following partial or complete corpus callosum section suggests that the corpus callosum is not the sole pathway for hemisphere synchronization. Experimental evidence suggests that a pathway between ipsilateral and contralateral cortex relayed via thalamic and mesencephalic subcortical structures may also contribute to secondary bilateral synchrony (Spencer et al., 1985).

Developmentally, the *tracé discontinu* and *tracé alternant* patterns of premature and full-term infants are analogous to burst suppression, in that bihemispheric suppression of activity occurs. Hahn et al. (1989) have postulated that the decrease in duration of interburst intervals with increasing gestational age is due to 'the loss of presumed subcortical systems responsible for the abrupt bihemispheric inhibition of cortical activity.'

Human and animal data demonstrate an increase in focal EEG abnormalities and focal seizures following callosal section. These findings lend support to the corpus callosum's contribution toward inhibition of cerebral activity, potentially through relay of inhibitory signals toward the ictal focus (Spencer et al., 1985).

In the clinical and experimental settings, the typical bilaterally synchronous burst suppression EEG pattern is thought

attributable to cortical isolation from afferent input originating in subcortical nuclei (Chatrian, 1990). In our patient, it could be argued that such functional ‘deafferentation’ was produced by barbiturate anesthesia. Our findings of asynchronous burst suppression with corpus callosum hemorrhage suggest that the corpus callosum plays a fundamental role in the synchronization of EEG activity in the two hemispheres, even under the extreme conditions of burst suppression due to barbiturates. When the corpus callosum was severed by hemorrhage, the burst suppression pattern became asynchronous. The association of asynchronous burst suppression with Aicardi’s syndrome (which includes partial or complete agenesis of the corpus callosum) supports such a role for the corpus callosum in interhemispheric synchrony (Fariello et al., 1977).

We might speculate that burst suppression does not derive from discharges arising in subcortical structures, but is in fact of cortical origin. One might propose that a burst suppression pattern secondary to cortical suppression with release of subcortical activity would likely be synchronous. Thus, asynchronous bursts would suggest that the primary pacemaker of the burst suppression pattern is cortical in origin.

In conclusion, we propose that asynchronous burst suppression under pentobarbital anesthesia in our patient with a corpus callosum hemorrhage occurred because: (1) normally, the corpus callosum modulates interhemispheric synchronization of cortical inhibition; and (2) cortical areas were ‘released’ from such synchronization due to disruption of the corpus callosum.

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