Seizure 22 (2013) 908–910

Contents lists available at SciVerse ScienceDirect

Seizure

journal homepage: www.elsevier.com/locate/yseiz

Clinical letter

Postictal bradyarrhythmia following an isolated seizure in a patient with left hemisphere stroke

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ARTICLE INFO

Article history:
Received 1 May 2013
Received in revised form 10 June 2013
Accepted 19 June 2013

1. Case report

Sudden death contributes significantly to mortality in patients with refractory epilepsy and acute stroke.[1,2] Presently, our field has only a rudimentary understanding of the pathophysiology underlying these phenomena, and proposed substrates include lethal centrally mediated cardiac arrhythmias.

A 73-year-old diabetic hypertensive woman with atrial fibrillation (not anticoagulated due to recent severe epistaxis) presented to our emergency ward for new onset slurred speech, drooling and difficulty producing words. On examination, she was agitated, hypertensive to 209/132, and in atrial fibrillation at a rate of 118. She displayed a predominantly receptive aphasia with dysarthria and right hemineglect, as well as right hemianopsia and a mild right hemiparesis. A noncontrast head computed tomography scan showed no hemorrhages or conspicuous hypodensities. Thrombolysis was deferred as the time of onset of symptoms was unknown. Presumed to have a left hemisphere embolic stroke, she was admitted to the neurointensive care unit and heparinized.

The next morning, she was somnolent and difficult to arouse. She was placed on continuous video electroencephalography (cvEEG), which revealed a low voltage delta activity with superimposed theta and alpha over the right hemisphere. Background activity in the left hemisphere was severely suppressed with extremely low voltage 1–2 Hz activity. Over the next several hours, she displayed occasional spike and slow wave discharges with phase reversal at C3 and T3 electrodes that gradually increased in frequency and occurred in bursts lasting 2–3 s. Approximately 24 h into her ICU stay, she displayed a clinical seizure characterized by forced head deviation to the right, clonic jerking of her right and then bilateral limbs followed by generalized tonic posturing. Electrographically, this event was characterized by initial left hemisphere high voltage rhythmic sharp delta activity with superimposed beta activity that evolved into high voltage rhythmic polyspikes which then spread to the right hemisphere (Fig. 1). Following the seizure, severe bilateral attenuation was observed on EEG. Ictally, cardiac telemetry revealed frequent premature ventricular contractions in the background of an irregularly irregular rhythm. This was followed immediately by atrial flutter with an extremely slow ventricular response at 20–30 bpm, concurrent with significant hypotension (40–50/palp). Her oxygen saturations remained within normal limits and blood gas measurements identified acidosis without hypoxemia (7.00/78/74). Her cardiac rhythm reverted to her baseline atrial fibrillation rhythm only after multiple rounds of atropine and epinephrine injections and five minutes of transcutaneous cardiac pacing. She was endotracheally intubated and placed on pressor support. A bedside echocardiogram identified no regions of focal hypokinesis with grossly preserved systolic function, and a serum troponin level returned at 0.03 ng/ml (increased from 0.02 ng/ml before her seizure). Given the possibility of diffuse anoxic brain injury, she was empirically cooled down to 33 °C for 24 h per our institution's post-cardiac arrest therapeutic hypothermia protocol. Levetiracetam was initiated intravenously.

Thirty-six hours after her isolated seizure, her EEG demonstrated a burst suppression pattern. Magnetic resonance imaging demonstrated patchy areas of infarction in the distribution of the left middle cerebral and posterior cerebral artery distributions in the background of chronic microvascular ischemic changes (Fig. 2a and b). Her course deteriorated over the next 10–11 days, as she developed oliguric renal failure and sepsis with a ventilator-associated pneumonia. There were no

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http://dx.doi.org/10.1016/j.seizure.2013.06.009

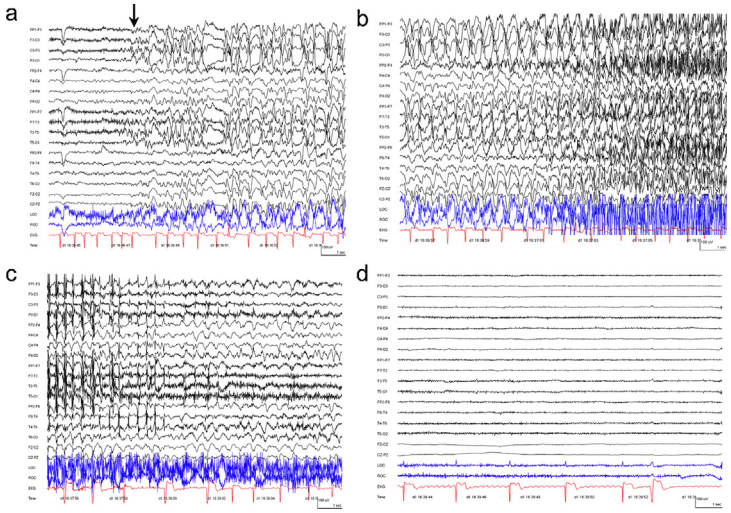

Fig. 1. Electroencephalogram tracings accompanied by electrocardiographic telemetry data (red tracings) with timestamps (e.g., d1 16:37:58, corresponds to 4:37 pm on Day 1 of recording). (a) The patient's seizure begins over the left hemisphere (arrow, 16:36:48), while in atrial fibrillation at a rate of approximately 70–80 bpm. (b) Ictal rhythmic delta activity spreads from the left to the right hemisphere. (c) Electrographically, generalized rhythmic activity terminates in approximately 70 s (16:38:00) at which point the patient's cardiac rhythm transforms into atrial flutter with a slow ventricular response. Rhythmic delta activity in the right hemisphere persists until approximately 16:38:38. (d) Post ictal generalized EEG suppression is noted starting at approximately 16:39:44. The patient remained in this bradyarrhythmia with hypotension until the administration of transcutaneous pacing and intravenous pressor therapy. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

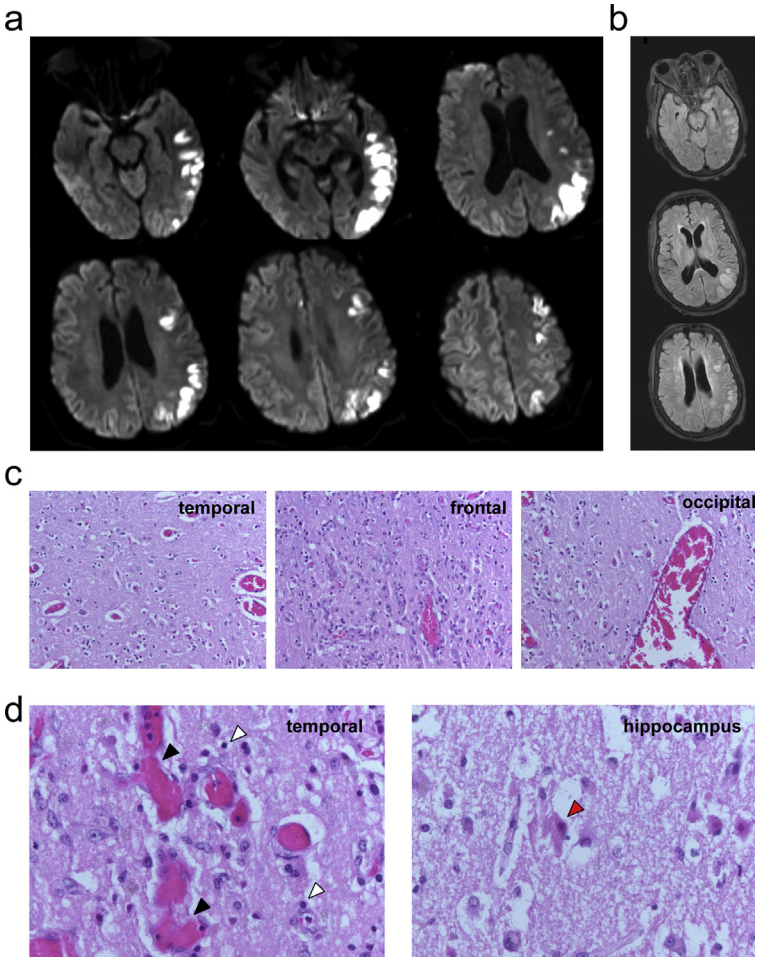

Fig. 2. (a) Post-cooling axial diffusion weighted MR images demonstrating patchy areas of restricted diffusion in the left temporal and occipital lobes. (b) Axial FLAIR (fluid attenuated inversion recovery) sequences demonstrating corresponding areas of FLAIR hyperintensity together with periventricular hyperintensities suggestive of chronic microvascular ischemic changes. (c) 20× magnified representative light microscopic images of hematoxylin/eosin (H/E) stained views of the left temporal, frontal and occipital cortices demonstrating ischemic neuronal loss of neurons and reactive gliosis. (d) 40× magnified views of the left temporal cortex and left hippocampus demonstrating hypertrophic dilated microvasculature (filled triangles) and monocytic infiltrates (white triangles) in the background of scattered hypereosinophilic neurons (red triangle). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

further convulsions noted, but her neurological examination remained poor without purposeful movements or spontaneous awakening. Following a lengthy discussion with the patient's family, comfort care measures were pursued and the patient expired peacefully approximately two weeks following her acute stroke.

Brain autopsy identified extensive intracranial atherosclerosis without herniation, occult hemorrhages or masses. Microscopic examination of the left temporal lobe demonstrated signs of ischemic hypoxic injury with laminar necrosis, hypertrophic dilated microvasculature and infiltrates of macrophages and monocytes. Ischemic changes were equally prominent in cortical regions unaffected by the stroke (e.g., left frontal cortex), consistent with a global hypoxic event (Fig. 2c and d).

2. Discussion

In this case, a single seizure arising from a left hemispheric focus secondarily generalized. We propose that a seizure-induced relative excess in parasympathetic activity resulted in atrioventricular nodal blockade transforming her atrial fibrillation into a flutter rhythm with an extremely slow ventricular response. This arrhythmia persisted well after her electrographic seizure had terminated. The resultant hypotension and impaired cerebral perfusion resulted in diffuse anoxic brain injury, manifested electroencephalographically as delayed suppression transitioning into burst suppression patterns. Autopsy findings also confirmed diffuse areas of cell loss and gliosis consistent with anoxic damage.

Both tachyarrhythmias and bradyarrhythmias can occur within the context of a seizure, but the latter are significantly less common,[3] occurring either due to apnea and associated hypoxemia, or from a primary ictal phenomenon. Advances in neuroimaging, continuous EEG and telemetry, combined with seminal electrical stimulation experiments have led to the appreciation of a network of cortical and subcortical brain regions involved in the central control of the autonomic nervous system.[2] Ictal activity within these regions, including bilateral insular and anterior cingulate cortices, the amygdala, thalamus and the hypothalamus, is believed to generate these arrhythmias.[1] A lateralization hypothesis has been proposed whereby right hemisphere activation leads to sympathetically driven tachyarrhythmias, whereas left hemispheric activation produces parasympathetic effects with significant bradyarrhythmias.[1–3] The seizure described in this report obeys this model. Peri-ictal bradyarrythmias have been proposed to be one of many substrates of SUDEP (sudden unexpected death in epilepsy), and may be a consequence of centrally mediated parasympathetic surges or the hypoxemia that results from ictal central apnea. SUDEP typically affects patients with longstanding refractory generalized convulsions. Our case is unique in that our patient did not have epilepsy: a *single* seizure generated a profound bradycardia, suggesting that the pathological substrates responsible for malignant ictal arrhythmias do not require a lengthy "maturation period" through repeated epileptic seizures.

Ischemic stroke also raises the risk of sudden death, and pathophysiological explanations have revolved around two key themes: (1) "neurogenic" myocardial injury occurring in patients with pre-existing coronary artery disease, and (2) autonomic dysregulation occurring at the time of stroke in the presence of premorbid abnormalities in ventricular repolarization, such as a prolonged QT interval.[2] Compared with right-sided infarctions, left-sided infarctions are associated with an increased risk of sudden death.[4] Our case demonstrates the very real and previously unappreciated possibility that seizures during this acute period may result in sudden death through the epileptic activation of the central autonomic network and resultant lethal brady- or tachyarrhythmias. Furthermore, it highlights the key role of electroencephalography in the neurointensive care unit as a means to provide greater insights into our understanding of the central control of cardiac function.

Disclosure

The authors declare no competing financial interests.

References

1. Sevcencu C, Struijk JJ. Autonomic alterations and cardiac changes in epilepsy. *Epilepsia* 2010;**51**:725–37.
2. Soros P, Hachinski V. Cardiovascular and neurological causes of sudden death after ischaemic stroke. *The Lancet Neurology* 2012;**11**:179–88.
3. Jansen K, Lagae L. Cardiac changes in epilepsy. *Seizure* 2010;**19**:455–60.
4. Algra A, Gates PC, Fox AJ, Hachinski V, Barnett HJ. Side of brain infarction and long-term risk of sudden death in patients with symptomatic carotid disease. *Stroke* 2003;**34**:2871–5.