Journal of Investigative Medicine High Impact Case Reports
Volume 8: 1–11

DOI: 10.1177/2324709620940497
journals.sagepub.com/home/hic
SAGE

Stroke-Onset Seizures During Midbrain Infarction in a Patient With Top of the Basilar Syndrome

Edward C. Mader Jr., MD[1], Vaniolky Losada, MD[1], Jessica C. Baity, MD[1], Ebony M. McKinnies, MD[1], and Lionel A. Branch, MD[1]

Abstract

Risk factors for early-onset seizures in acute ischemic stroke include anterior circulation stroke, infarction of the cerebral cortex, large infarct size, and ischemic-to-hemorrhagic transformation. We define stroke-onset seizures as seizures occurring within 2 hours of stroke onset. A 64-year-old woman presented with top of the basilar artery syndrome—thalamic infarction occurred first and midbrain infarction 12 days later. She manifested stroke-onset seizures during midbrain infarction, which was heralded by stupor. Within 2 hours of the onset of stupor, she had a clonic seizure of the lower extremities, electroencephalography (EEG) revealed nonconvulsive status epilepticus, and an episode of convulsive movements of all extremities was recorded on video and on EEG. Continuous EEG recording showed epileptiform discharges that would appear, disappear, and reappear over a 3-week period. It took 3 weeks and 4 antiepileptic drugs to fully suppress cortical hyperexcitability, perhaps because injury to some midbrain structures resulted in global lowering of the seizure threshold. The most important risk factor for stroke-onset seizures appears to be posterior circulation stroke, particularly brainstem infarction. The difference in risk profile between stroke-onset seizures and other forms of early-onset seizures suggest that their pathophysiology is not exactly the same. Focusing some of the research spotlight on stroke-onset seizures can help us better understand their unique clinical, electrographic, radiologic, and pathophysiologic features.

Keywords

seizure, status epilepticus, early onset, ischemic, stroke, midbrain, thalamus, basilar

Introduction

Approximately 5% of patients with acute ischemic stroke manifest convulsive seizures, of which 10% to 20% meet the criteria for status epilepticus.[1-3] Nonconvulsive seizures has been detected with scalp electroencephalography (EEG) in <5% of patients with acute ischemic stroke.[4,5] In comparison, continuous EEG (cEEG) can detect nonconvulsive seizures or nonconvulsive status epilepticus (NCSE) in 9% to 18% of patients with severe ischemic stroke and coma.[6,7] The occurrence of seizures in stroke is associated with higher mortality, worsened recovery, and poststroke epilepsy.[8,9] Because cEEG is resource-intensive, this procedure cannot be offered to all patients with acute ischemic stroke, most of whom have a low risk of nonconvulsive seizures.[10,11] More realistically, cEEG should be performed in acute ischemic stroke patients with a high risk of nonconvulsive seizures, including those with stupor/coma, extensive cortical infarcts, or hemorrhagic transformation.[12]

Poststroke seizures are designated as *early-onset seizures* if they occur within 2 weeks of the onset of stroke and as *late-onset seizures* if they occur after 2 weeks.[13] The choice of 2 weeks as cutoff has no clear pathophysiological basis. Gupta et al found that 30% of postinfarction seizures are early-onset seizures and 90% of early-onset seizures are day-1 seizures.[14] In a prospective multicenter study of seizures after stroke, Bladin et al concluded that 4.8% of patients with ischemic stroke experienced early-onset seizures, and in 40% of these patients (~2% of patients with ischemic stroke), the early-onset seizure was a day-1 seizure.[15] However, their study included only hemispheric strokes because of a prior study that showed no correlation between seizures and brainstem strokes. Risk factors for early-onset seizures in ischemic stroke include cortical injury, large infarct size, involvement of the anterior

[1]Louisiana State University Health Sciences Center, New Orleans, LA, USA

Received May 6, 2020. Revised June 8, 2020. Accepted June 10, 2020.

Corresponding Author:
Edward C. Mader, Department of Neurology, Louisiana State University Health Sciences Center, 1542 Tulane Avenue, New Orleans, LA 70112, USA.
Email: emader@lsuhsc.edu

circulation or temporal lobes, and hemorrhagic transformation of the infarct.[16]

Some studies of early-onset seizures examined seizures that occurred close to the time of stroke onset. In a community-based study of poststroke seizures, Burn et al designated seizures occurring within 24 hours of stroke onset as *onset seizures*.[17] Different authors used the term *seizure at stroke presentation* (SSP) as a label for different types of early-onset seizures. Huang et al defined "seizures occurring within 24 hours of stroke onset" as SSP and found that 1.53% of ischemic stroke patients had SSP.[8] Abend et al considered "any seizure observed by a parent, guardian, or medical provider occurring as the heralding sign of the stroke or within 1 hour of the onset of stroke" as SSP; the authors detected SSP in 22% of children with arterial ischemic stroke.[18] By restricting the definition of SSP to "any clinically evident seizure observed by a parent/guardian or medical provider occurring as the heralding sign of the stroke," Cheng et al concluded that ischemic stroke patients with SSP had a higher incidence of posterior circulation infarction than their non-SSP counterpart.[19]

The time of seizure occurrence in relation to the onset of stroke can have special pathophysiologic and therapeutic implications. Early-onset seizures can be labeled as *day-1 seizures* if the first seizure occurred within the first 24 hours of the onset of stroke and as *post day-1 seizures* if the first seizure occurred between 24 hours and 2 weeks after the onset of stroke. Furthermore, day-1 seizures that occur in close proximity to the onset of stroke can be labeled as *stroke-onset seizures*. We define stroke-onset seizures as seizures occurring within a time window—from 2 hours before to 2 hours after the onset of stroke. Our 4-hour time window is purely arbitrary and is not grounded on pathophysiology. We describe a case of stroke-onset seizures during acute ischemic stroke of the midbrain to illustrate how stroke-onset seizures might differ from other early-onset seizures.

Case Presentation

A 64-year-old woman was brought to the emergency room after being found unresponsive. According to her husband, she was normal when she woke up that morning. She was ready to leave the house to go to work. Instead, she was found slumped on the couch with eyes open but speechless and unable to follow commands. There was no injury, incontinence, or other signs to suggest that she had a seizure. The stroke code was immediately activated when she arrived in the hospital. She appeared lethargic with lack of interest in her environment, slow responses to stimulation, and a tendency to fall asleep. Blood pressure was 131/91 mm Hg, pulse rate 78 beats/min, respiratory rate 15 breaths/min, and oxygen saturation 99.8%. She was afebrile (37.1 °C) with no signs of meningeal irritation. Both pupils were 4 mm and equally reactive to light. There was no evidence of ophthalmoplegia, facial asymmetry, and other cranial nerve deficits. She moved all her extremities spontaneously and to the same degree. Her biceps, triceps, brachioradialis, patellar, and ankle reflexes were all 1+; she had no ankle clonus; and Babinski sign was absent. Past history was positive for atrial fibrillation and right frontal ischemic stroke, but negative for seizures/epilepsy. Four years prior to admission, she survived a cardiac arrest, received a pacemaker/defibrillator, and fully recovered. Computed tomography (CT) of the head showed an area of encephalomalacia in the right frontal lobe consistent with her old stroke (Figure 1). Electrocardiogram showed regular atrial-sensed ventricular-paced rhythm with a rate of 80 beats/min. Nonconvulsive seizures/status epilepticus was ruled out by stat EEG. Other studies, including blood counts, blood chemistry, and chest X-ray were normal. Because there was no clear evidence of a new stroke, tissue plasminogen activator was not administered.

The patient, who was initially lethargic (GCS [Glasgow Coma Scale] = 13), became stuporous (GCS = 10). She was intubated for airway protection and admitted to the intensive care unit. Magnetic resonance imaging could not be performed because of her pacemaker. Repeat head CT 12 hours later revealed bilateral paramedian thalamic infarcts and CT angiography showed filling defects at the top of the basilar artery and the P1 segments of the posterior cerebral arteries (Figure 1). The possibility of an occluded artery of Percheron could not be ruled out. Telemetry showed regular ventricular-paced rhythm with a rate of 64 to 80 beats/min. Pulse oximetry consistently showed oxygen saturations ≥99.0%. Transthoracic echocardiography with bubble study was unrevealing. Transesophageal echocardiography was attempted but aborted because of failure to intubate the esophagus. Clopidogrel was added to aspirin (she has been taking aspirin for years since she had a stroke). Intravenous levetiracetam was administered empirically: 20 mg/kg was loaded followed by 500 mg q12h. However, cEEG recording over a 48-hour period only showed diffuse slowing and no signs of abnormal cortical hyperexcitability (Figure 2). Methylphenidate was started on day 3. She became progressively more alert and she started following simple commands. Extubation was attempted on day 6 but failed due to upper airway edema. She underwent tracheostomy and percutaneous endoscopic gastrostomy on day 9.

On day 12, the patient lapsed into stupor again (GCS = 9). Her blood pressure was 144/95 mm Hg, pulse rate 72 beats/min, respiratory rate 18 breaths/min, and oxygen saturation 99.1%. Telemetry showed normal rate and rhythm. Blood test results were as follows: white blood cells count = $7.8 \times 10^3/\mu L$, hemoglobin = 12.8 gm/dL, red blood cells count = $4.56 \times 10^6/\mu L$, platelets = $235 \times 10^3/\mu L$, sodium = 142 mmol/L, potassium = 4.1 mmol/L, magnesium = 2.2 mg/dL, chloride = 110 mmol/L, CO_2 = 30 mmol/L, glucose = 104 mg/dL, BUN (blood urea nitrogen) = 24 mg/dL, creatine = 0.82 mg/dL, total protein = 7.2 g/dL, albumin = 3.6 g/dL, ammonia = 32 μg/dL, aspartate aminotransferase = 16 U/L, alanine aminotransferase = 14

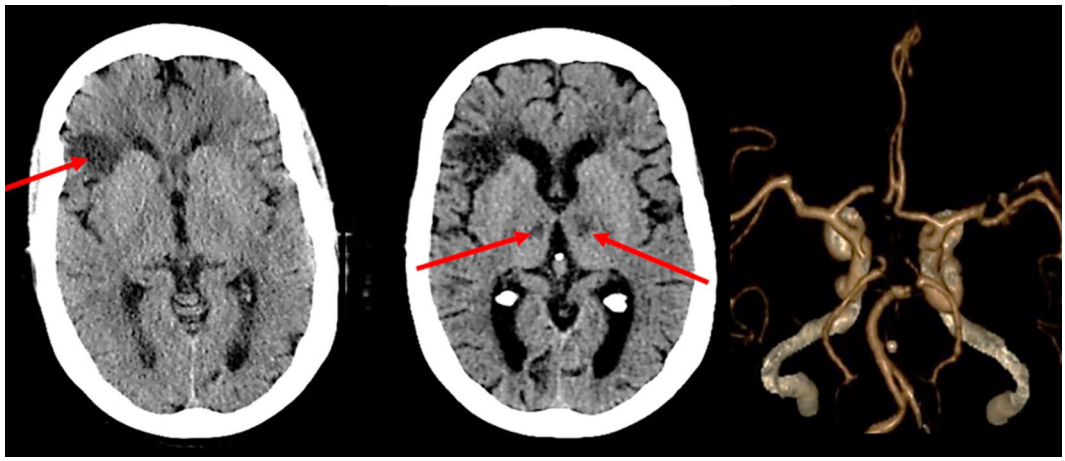


Figure 1. Initial computed tomography (CT) scan of the head (left) showed an area of encephalomalacia in the right frontal lobe (arrow) consistent with an old stroke. Repeat CT scan of the head (middle) 12 hours after the initial CT scan revealed acute infarcts in the paramedian zone of the thalami (arrows) and CT angiogram (right) showed filling defects at the top of the basilar artery and the P1 segments of the posterior cerebral arteries.

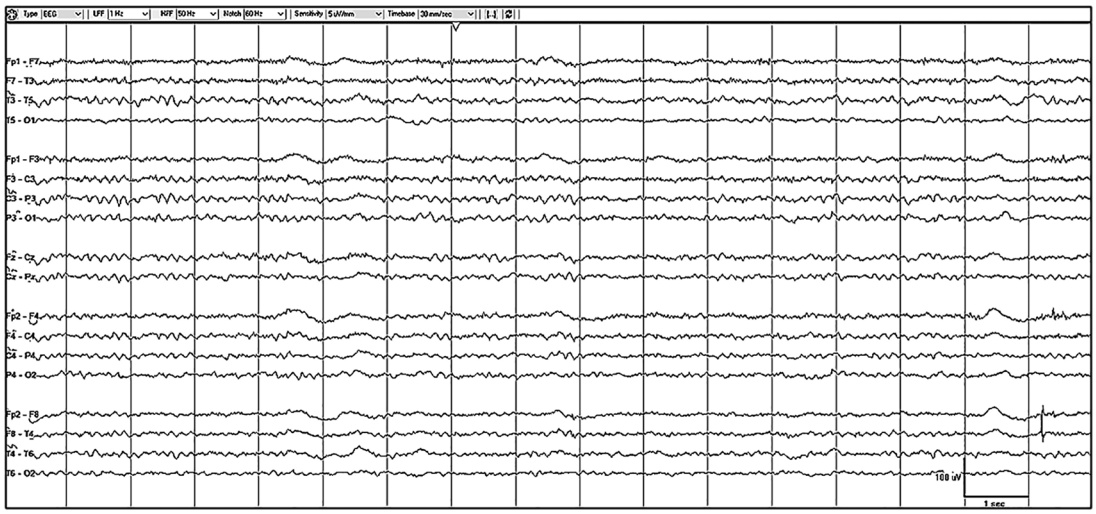
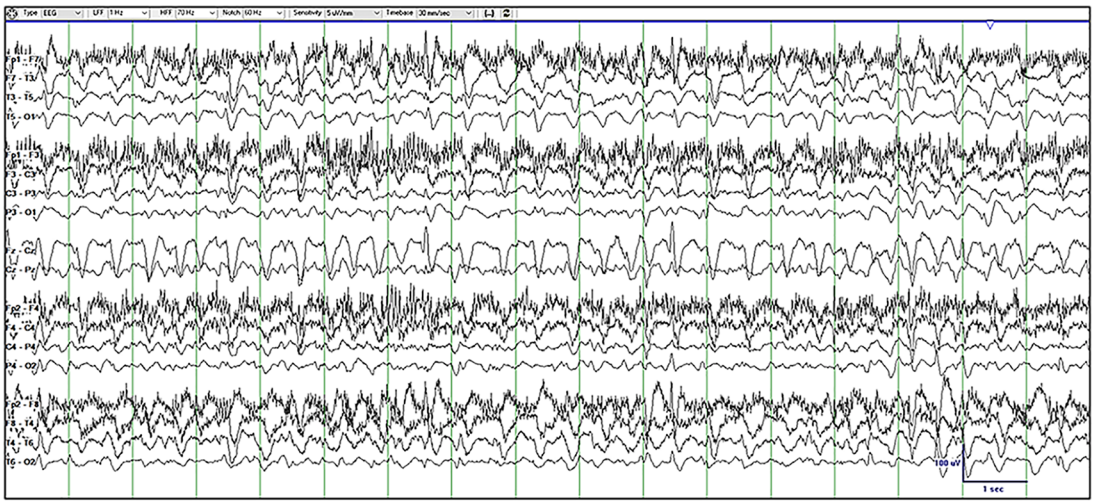
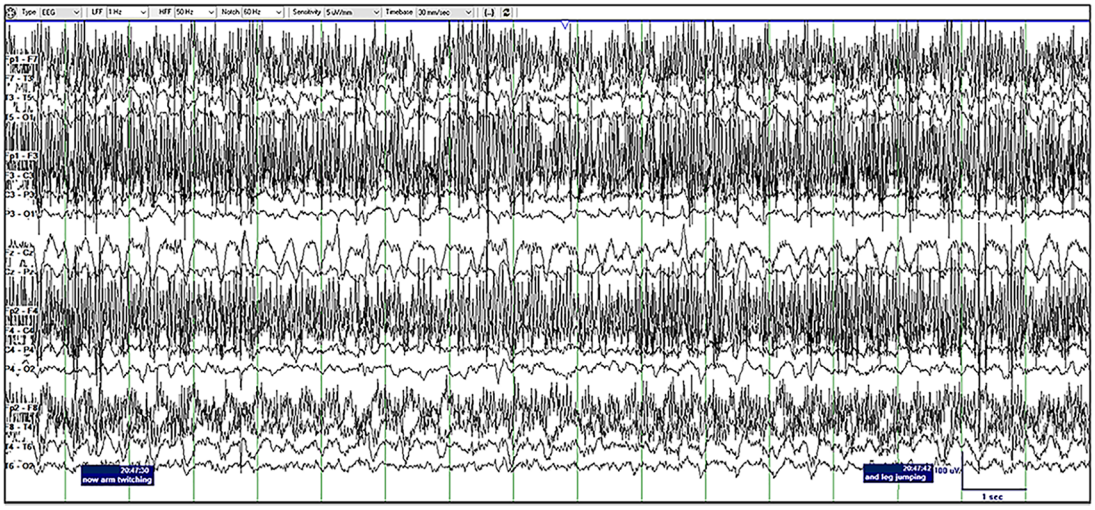


Figure 2. Two days of continuous electroencephalography (days 2 and 3) showed generalized slowing, mainly rhythmic theta activity, with superimposed low-voltage semirhythmic and nonrhythmic delta activity. No epileptiform discharges, electrographic seizures, or periodic discharges were detected.

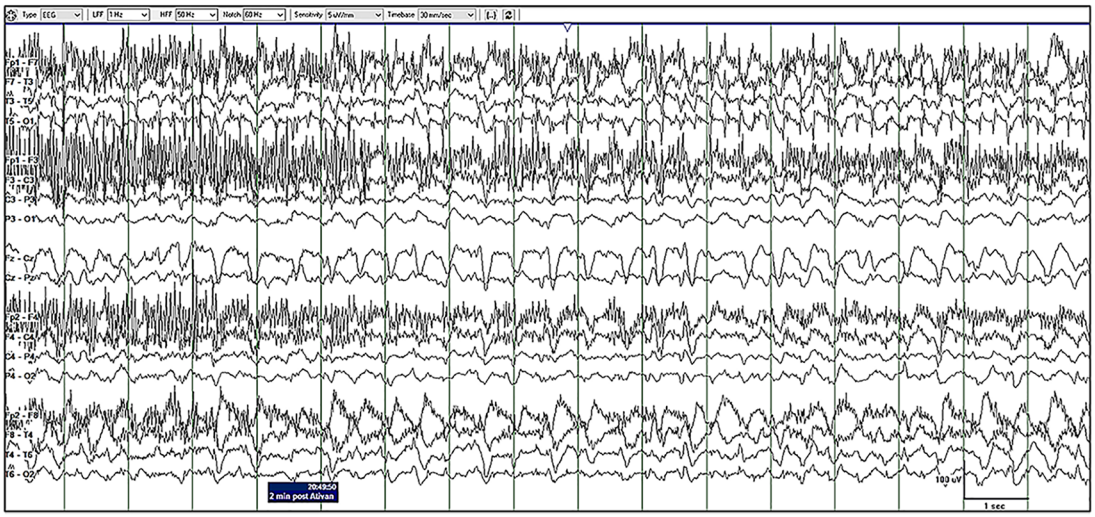
U/L, alkaline phosphatase = 75 U/L, bilirubin = 0.2 mg/dL, and thyroid stimulating hormone = 0.95 μIU/mL. With metabolic, renal, and hepatic parameters in the normal range and no evidence of infection, the change in mental status could not be accounted for by a toxic, metabolic, or septic encephalopathy. Her husband noticed a 30-second episode of bilateral leg jerking (~30 minutes from onset of stupor). EEG recording (~80 minutes from onset of stupor) showed sustained generalized epileptiform discharges in the form of high-voltage rhythmic sharp and slow wave complexes (Figure 3A). The EEG findings satisfy the Salzburg criteria for NCSE.[20] She was initially awake and motionless but her extremities started jerking—rhythmic pronation-supination of the forearms occurred first, then rhythmic hip and knee flexion-extension. As seen on video, the movements were consistent with clonic/convulsive seizure lasting 28 seconds. The EEG, which was obscured by muscle artifact, did not show any significant change other than a slight increase in the frequency of epileptiform discharge from 2 to 2.5 Hz (Figure 3B). Lorazepam 2 mg was



A



B



C

Figure 3. *(continued)*

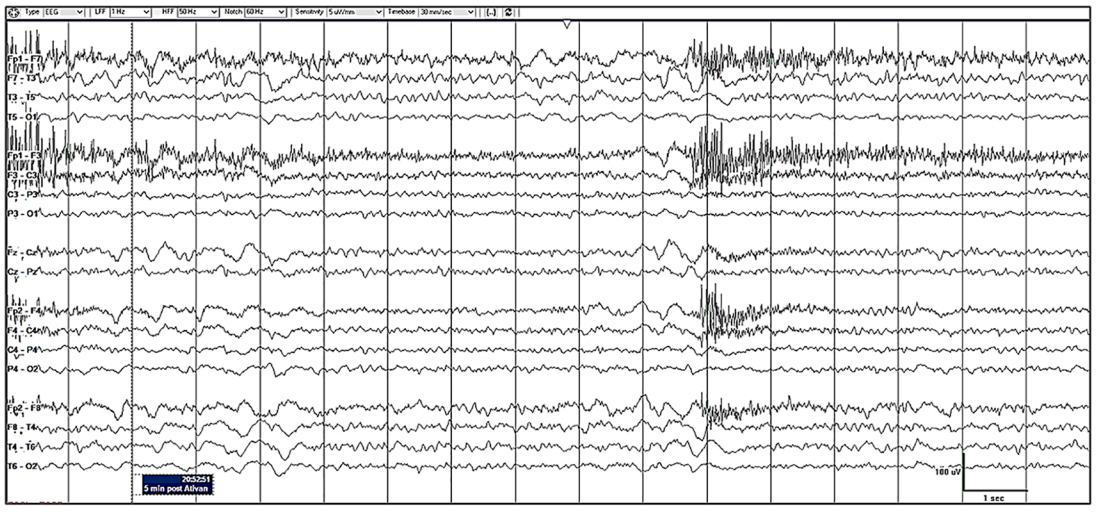


Figure 3. (A) Before convulsive movements. (B) During convulsive movements. (C) 2 minutes after lorazepam injection. (D) 5 minutes after lorazepam. Electroencephalography recorded approximately 80 minutes from the onset of stroke (before the convulsive episode) showed generalized rhythmic 2-Hz sharp wave and slow wave complexes (A). Despite abundant myogenic artifact, the EEG during convulsion continued to show similar epileptiform discharges with a slightly higher frequency of 2.5 Hz (B). Convulsive movements stopped even before lorazepam was injected. After lorazepam 2 mg was administered, the epileptiform discharges started to decrease in frequency (C) and subsequently dissipated (D).

injected resulting in attenuation and dissipation of epileptiform discharges (Figure 3C and D). Stupor was attributed to NCSE but midbrain infarction was also a concern. When this possibility and its prognostic implications were discussed with her family, they decided against further invasive interventions.

Approximately 3 hours from the onset of stupor, signs of a right third nerve palsy (ptosis and dilated nonreactive pupil) became evident. Stat CT of the head showed the same infarct in the paramedian zones of the thalami with no midbrain infarct (Figure 4, top row). Repeat CT of the head (~22 hours after the onset of stupor) showed extension of the infarct from the paramedian zones of the thalami to the paramedian zones of the midbrain with greater involvement of the right side consistent with the clinical findings of stupor and right oculomotor nerve palsy (Figure 4, bottom row). cEEG showed waxing-waning generalized epileptiform discharges consistent with relapsing and remitting cortical hyperexcitability or NCSE (Figure 5). Although cEEG showed periods of generalized slowing with no epileptiform discharges these "nonictal" periods were frequently superseded by longer "ictal" periods lasting 1 to 4 hours. The typical sequence consisted of a build-up of rhythmic delta activity, an increasing density of sharp waves, and evolution toward more organized and rhythmic 1.5 to 2.5 Hz high-voltage sharp and slow wave complexes. The epileptiform discharges tend to persist for hours with minor fluctuations in frequency, amplitude, and morphology before breaking up and dissipating (Figure 5). While her ability to respond was limited to following simple commands, she was more somnolent and less responsive every time high-voltage rhythmic discharges appeared in the EEG. Focal electrographic seizures did not occur, but her husband witnessed 2 more episodes of bilateral leg jerking, both of which were similar to the first episode. Only the last episode was recorded: there was no discernible change in the EEG during the leg movements. Increasing the dose of levetiracetam and phenytoin and intermittent boluses of lorazepam temporarily suppressed NCSE. After several hours, NCSE would reemerge, first appearing as generalized rhythmic delta activity with no clear ictal features, but gradually gaining more "ictal" features, such as an increase in discharge frequency, amplitude, and sharpness. While cEEG was omitted for 5 days during the 3-week period, it is reasonable to assume that the patient was in and out of NCSE, or in some state of cortical hyperexcitability within the ictal-interictal continuum, over a period of 3 weeks. Of note, the patient's family refused the induction of coma with anesthesia, such as propofol. Adding sodium valproate to her antiepileptic regimen resulted in suppression of epileptiform activity. She became more alert and responsive at that point, though she remained nonverbal and only followed simple commands. On hospital day 33, she was discharged to a long-term acute care facility.

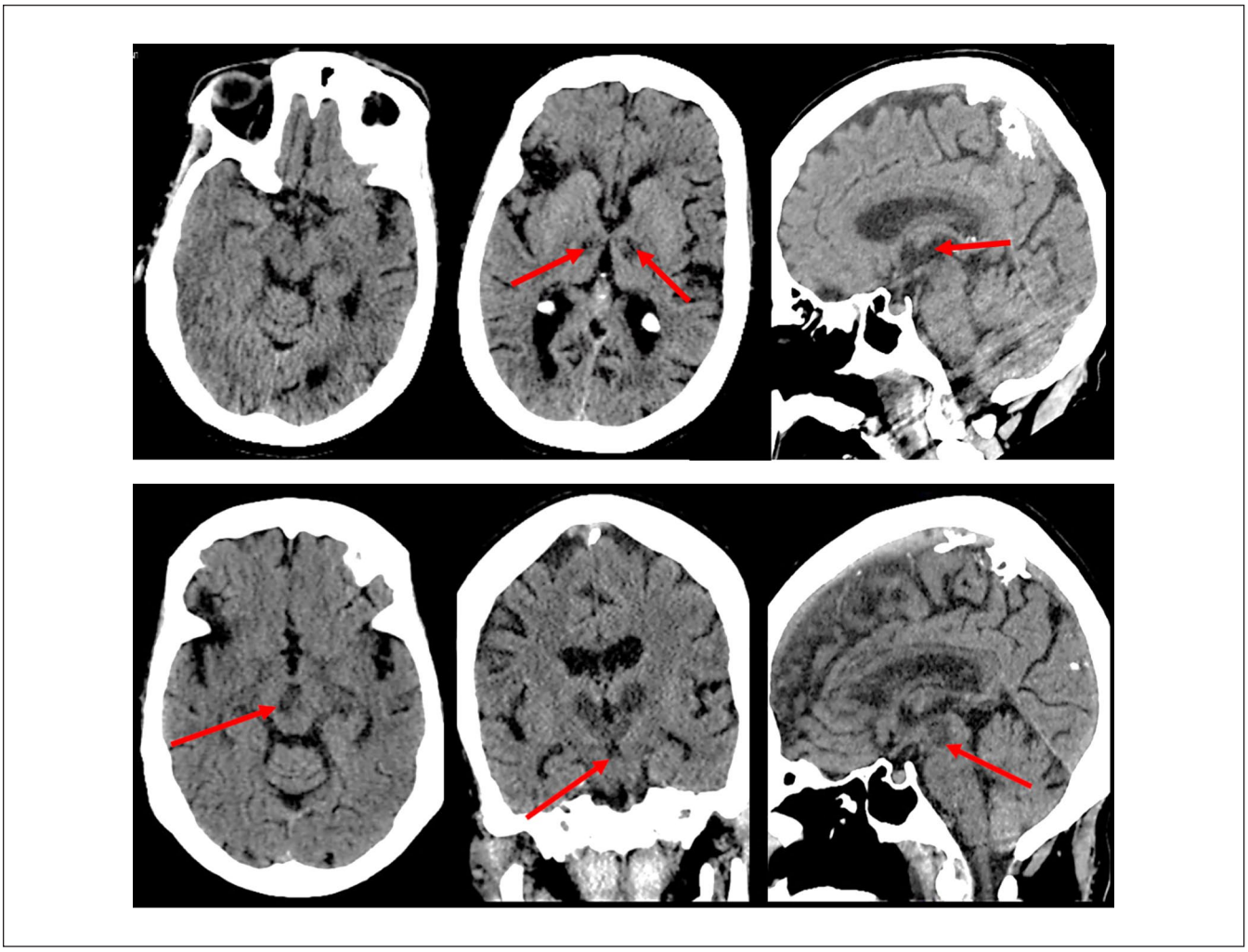
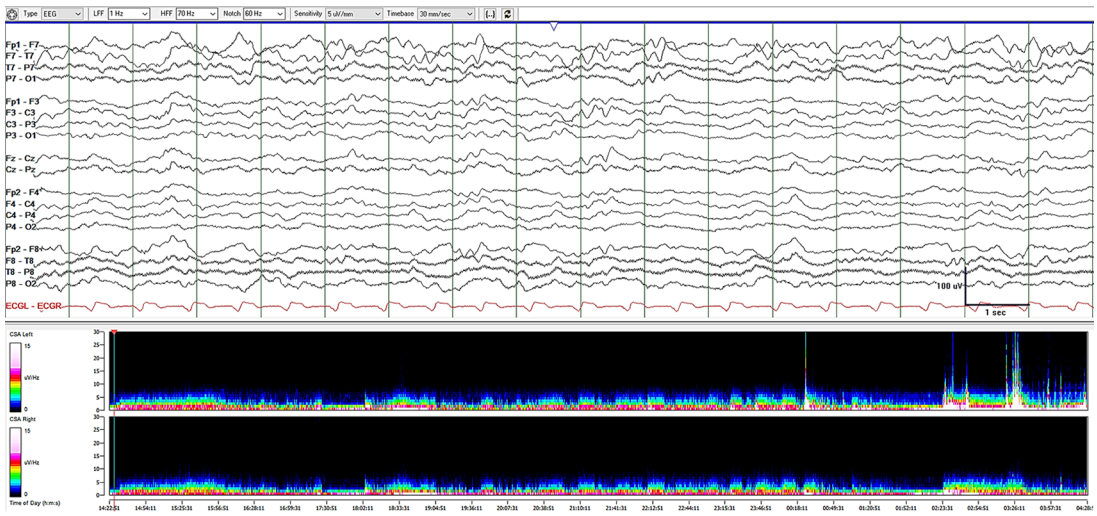


Figure 4. Computed tomography (CT) scan of the head on day 12 (top row), 4 hours after the onset of stupor and 1 hour after appearance of oculomotor nerve palsy, showed the previous infarct in the paramedian zones of the thalami (arrows) with no clear-cut involvement of the midbrain. Repeat CT scan of the head on day 13 (bottom row), 22 hours after the onset of stupor, showed extension of the infarct from the paramedian zones of the thalami to the paramedian zones of the midbrain with greater involvement of the right side (arrows) consistent with the clinical findings of stupor and right oculomotor nerve palsy.

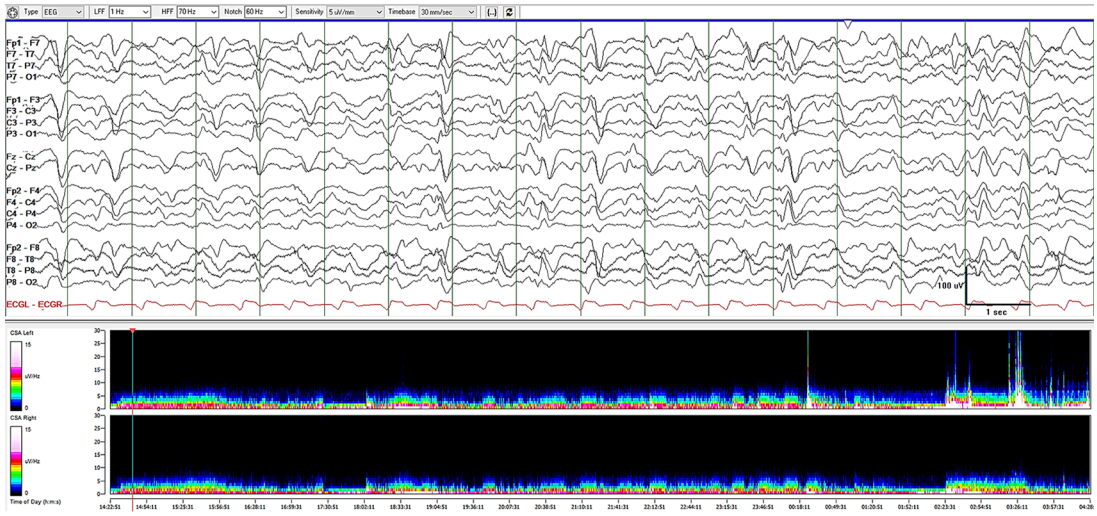
Discussion

In the case presented, thrombotic occlusion of the top of the basilar artery resulted in paramedian thalamic infarction followed, 12 days later, by paramedian midbrain infarction. The patient did not have seizures at any time before, during, and 12 days after thalamic infarction. Stroke-onset seizures occurred within 2 hours of midbrain infarction (estimated based on the time of onset of stupor), including (1) clonic seizure of the legs (witnessed by her husband), (2) NCSE (recorded on EEG), and (3) clonic seizure involving all extremities (recorded on video and EEG). The latter occurred during NCSE. The same NCSE pattern persisted during the convulsive movements. Early-onset, but not stroke-onset, seizures also occurred, including repeated emergence of NCSE (recorded during cEEG) and 2 more clonic seizures of the legs (witnessed by her husband). Of the 3 clonic seizures of the legs, only the last episode was recorded during cEEG. There was no change in the EEG during leg jerking.

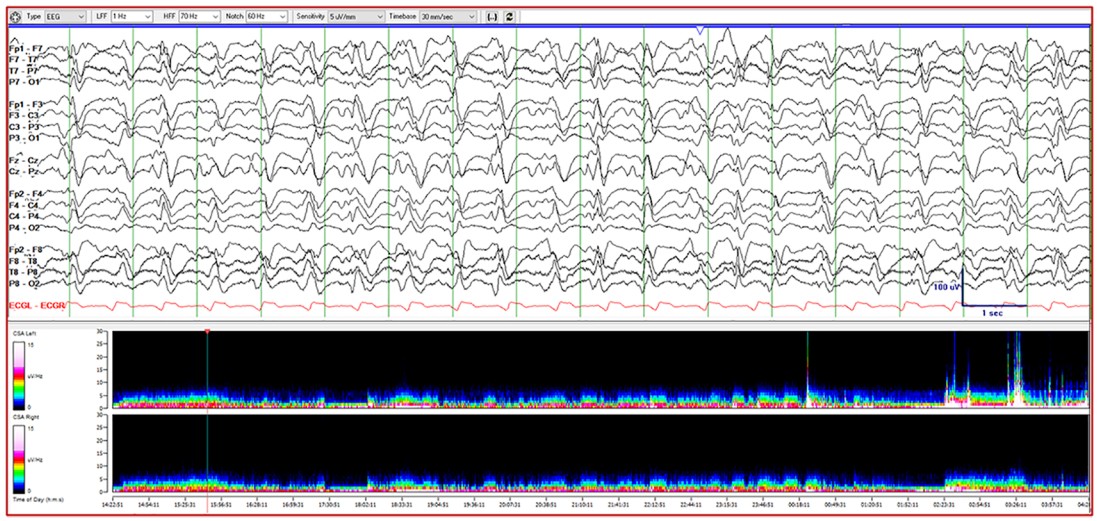
Several cases have been reported in the literature in which stroke-onset seizures occurred during acute infarction in the posterior circulation territory as a result of basilar artery occlusion or stenosis.[21-31] Infarction occurred in the paramedian thalamus, midbrain, or both thalamus and midbrain, except in one case where infarcts were detected in the cerebellum, medial temporal lobe, and occipital cortex, but not in the thalamus or midbrain. In the study of Cheng et al, where only stroke-onset seizures heralding the onset of stroke were considered as SSP (see Introduction), posterior circulation infarction was found in 25.7% of patients with SSP and in only 12.5% of patients without SSP.[20] Brainstem and thalamic lesions were more likely and temporal lobe



A

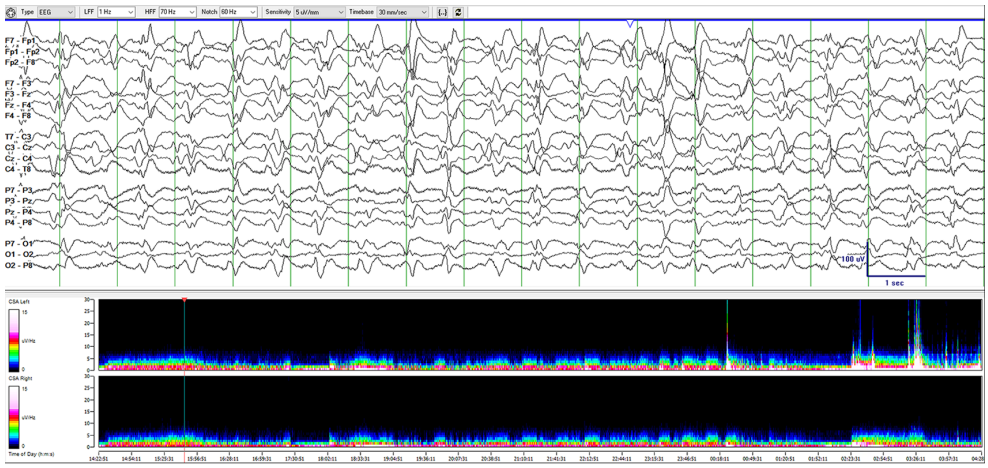


B



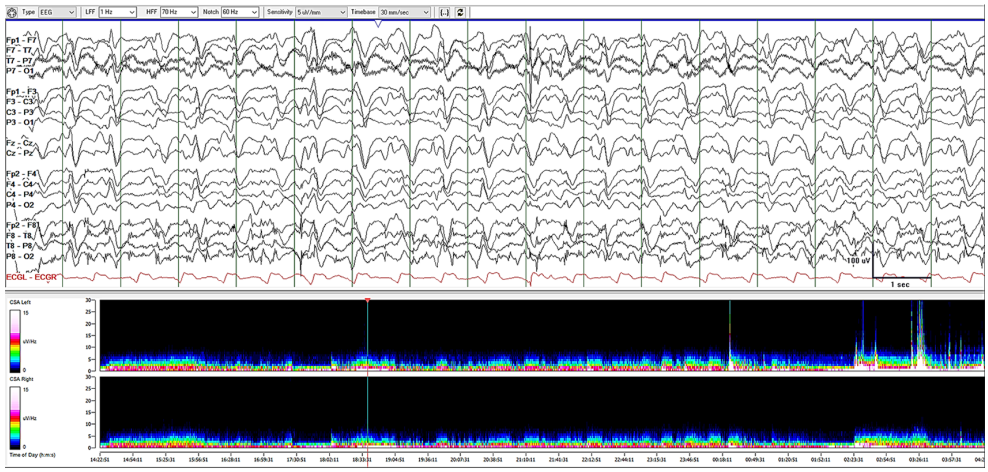
C

Figure 5. *(continued)*



D

E



F

Figure 5. (A) Generalized slowing with no epileptiform discharges. (B) Build-up of generalized rhythmic delta and sharp activity. (C) Clear-cut epileptiform discharges seen with longitudinal bipolar montage. (D) Same EEG tracing shown above displayed using transverse bipolar montage. (E) Epileptiform discharges start to break up and dissipate. (F) Next epoch with epileptiform discharges reappearing after <1 hour. Selected continuous electroencephalography epochs with compressed spectral array map (see line marker) showing waxing-waning cortical hyperexcitability. Sustained periods of generalized slowing with no epileptiform discharges (A) are followed by build-up of rhythmic delta and sharp wave activity (B) that evolve into clear-cut epileptiform discharges, as seen using longitudinal bipolar (C) and transverse bipolar montages (D), persisting over 1 to 4 hours, before breaking up and dissipating (E), only to return (F).

lesions were less likely in patients with SSP when compared with patients without SSP. Therefore, even though hemispheric/cortical infarcts are often implicated in early-onset seizures, brainstem infarcts may be more common in patients with stroke-onset seizures. The difference in risk profile between stroke-onset seizures and other forms of early-onset seizures suggest that the mechanisms of seizure generation and perpetuation may vary depending on where in the stroke timeline the seizure occurs.

The process by which acute ischemic stroke triggers early-onset seizures is not well understood. Evidently, tissue hypoperfusion/hypoxia (reperfusion may also be a factor) results in physiologic disturbances that interact to lower the seizure threshold and enhance the excitability of brain circuits.[32] Blood-brain barrier disruption, changes in neurotransmitter activity, perturbations in ion channel function, disturbances in electrolyte concentrations, and metabolic dysregulation have all been observed in the ischemic penumbra of an acute ischemic stroke.[32] Early-onset seizures have been studied in rodents using models of acute ischemic stroke, such as unilateral middle cerebral artery occlusion (MCAO) or photothrombotic ischemia.[33-37] Using the MCAO technique, Wu et al showed that deeper subcortical structures are crucial for generating convulsive seizures.[36] Zhang et al noted a striking similarity between convulsive seizures induced by the MCAO model and convulsive seizures induced by the hypoxia-ischemia model.[37] Interestingly, epileptiform discharges were recorded from brainstem areas but not from the hippocampi or neocortex. MCAO also produced nonconvulsive seizures with the ictal EEG showing epileptiform spikes in the hippocampi and neocortex.[37] While all animals with nonconvulsive seizures subsequently developed convulsive seizures, not all animals with convulsive seizures experienced a preceding nonconvulsive seizure. Animals that eventually developed convulsive seizures had worse outcomes than those with nonconvulsive seizures alone.

Convulsive motor activity can be an initial presentation of an impending basilar artery occlusion.[38] According to Saposnik and Caplan, convulsive-like movements in brainstem stroke are different from epileptic seizures and the sudden onset of a decerebrate posturing is often misinterpreted as a seizure.[39] As mentioned earlier, there are several reports of convulsive motor activity in association with basilar artery occlusion and infarction in which the authors interpreted convulsive activity as seizures.[21-31] It has been suggested that the sudden onset of convulsive or clonic movements, especially in patients with brainstem signs, should prompt the suspicion of a top of the basilar syndrome, whether the movements are considered seizures or not. The precise mechanism whereby infarcts in the posterior circulation produce seizure is still unknown. Penfield suggested a "centrencephalic system" in which the brainstem functioned as a causative center of seizures.[40] One proposed mechanism is disruption of inhibitory projections from the cortex to the brain stem. The extensive forebrain projections of the midbrain make it likely that various midbrain structures or circuits are directly involved in the global control of seizure threshold. Some midbrain structures may be involved in promoting ictogenicity, while other structures may have a role in preventing or terminating seizures. Arguably, destruction of midbrain structures responsible for increasing the seizure threshold or for terminating seizures could be the reason behind the refractoriness and pharmacoresistance of NCSE in our patient.

In orchestrating the complexities of seizure generation, the lead role is often given to the cerebral cortex. Nonetheless, convulsive seizures can be induced by electrical or chemical stimulation of the brainstem tegmentum.[41-43] The observation that convulsive seizures induced by stimulation of the mesencephalic reticular formation attenuate with pontine tegmentum lesions but are barely affected by precollicular transection suggest that the mesencephalic reticular formation plays a crucial role in the generation of convulsive seizures, perhaps by directly activating the descending reticular formation.[44] We also pointed out that Zhang et al recorded epileptic discharges from the brainstem, but not from the hippocampi or neocortex, during MCAO-induced convulsive seizures.[37] The stereotyped nature of the 4 clonic episodes in our patient and their rarity (only 1 episode of all-limb jerking and 3 episodes of leg jerking occurred over a 3-week period) point toward clonic seizures. However, the absence of a clear-cut change in the EEG during all-limb jerking and the absence of an ictal EEG correlate during leg jerking raise the possibility that the convulsive movements were not seizures. The absence of an ictal EEG correlate for the convulsive movements can be explained by the deep location of the generator in the medial cortical surface, by electrical potentials or artifacts making it difficult to detect the ictal discharges, by a dominant role of subcortical structures in generating the movements, or by a nonictal mechanism arising from the central pattern generators in the brainstem. We favor the first 2, but we also admit that we cannot rule out the third and fourth explanations.

Conclusion

Convulsive and nonconvulsive seizures/status epilepticus may occur at the onset of midbrain infarction. Pharmacoresistant seizure activity in the setting of midbrain injury suggests that some structures or circuits in the midbrain are crucial for seizure generation and perpetuation, whereas other structures are essential for seizure prevention and termination. The most important risk factor for stroke-onset seizures appears to be posterior circulation stroke, particularly brainstem infarction. The difference in risk profile between stroke-onset seizures and other forms of early-onset seizures suggest that their pathophysiology is not exactly the same. This should serve as motivation for researchers to examine stroke-onset seizures in greater detail.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

Ethics Approval

Our institution does not require ethical approval for reporting individual cases or case series provided that HIPAA identifiers are not present in the publication.

Informed Consent

Written informed consent was obtained from a legally authorized representative(s) for anonymized patient information to be published in this article.

ORCID iD

Edward C. Mader https://orcid.org/0000-0003-4516-2305

References

1. Lekoubou A, Bishu KG, Ovibiagele B. Mortality and trends in stroke patients with seizures: a contemporary nationwide analysis. *Epilepsy Res*. 2019;156:106166.
2. Wang JZ, Vyas MV, Saposnik G, Burneo JG. Incidence and management of seizures after ischemic stroke: systematic review and meta-analysis. *Neurology*. 2017;89:1220-1228.
3. Rumbach L, Sablot D, Berger E, Tatu T, Vuillier F, Moulin T. Status epilepticus in stroke: report on a hospital-based stroke cohort. *Neurology*. 2000;54:350-354.
4. Carrera E, Michel P, Despland PA, et al. Continuous assessment of electrical epileptic activity in acute stroke. *Neurology*. 2006;67:99-104.
5. Bentes C, Martins H, Peralta AR, et al. Post-stroke seizures are clinically underestimated. *J Neurol*. 2017;264:1978-1985.
6. Claassen J, Mayer SA, Kowalski RG, Emerson RG, Hirsch LJ. Detection of electrographic seizures with continuous EEG monitoring in critically ill patients. *Neurology*. 2004;62:1743-1748.
7. Scoppettuolo P, Gaspard N, Depondt C, et al. Epileptic activity in neurological deterioration after ischemic stroke, a continuous EEG study. *Clin Neurophysiol*. 2019;130:2282-2286.
8. Huang CW, Saposnik G, Fang J, Steven DA, Burneo JG. Influence of seizures on stroke outcomes: a large multicenter study. *Neurology*. 2014;82:768-776.
9. Camilo O, Goldstein LB. Seizures and epilepsy after ischemic stroke. *Stroke*. 2004;35:1769-1775.
10. Powers WJ, Rabinstein AA, Ackerson T, et al. Guidelines for the early management of patients with acute ischemic stroke: 2019 update of the 2018 guidelines for the early management of acute ischemic stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke*. 2019;50:e344-e418.
11. Herman ST, Abend NS, Bleck TP, et al. Consensus statement on continuous EEG in critically ill adults and children, part I: indications. *J Clin Neurophysiol*. 2015;32:87-95.
12. Kramer A, Kromm J. What is the role of continuous electroencephalography in acute ischemic stroke and the relevance of the“ ictal-interictal continuum”? *Neurocrit Care*. 2020;32:687-690.
13. Silverman IE, Restrepo L, Mathews GC. Poststroke seizures. *Arch Neurol*. 2002;59:195-201.
14. Gupta SR, Naheedy MH, Elias D, Rubino FA. Postinfarction seizures. A clinical study. *Stroke*. 1988;19:1477-1481.
15. Bladin CF, Alexandrov AV, Bellavance A, et al. Seizures after stroke: a prospective multicenter study. *Arch Neurol*. 2000;57:1617-1622.
16. Doria JW, Forgacs PB. Incidence, implications, and management of seizures following ischemic and hemorrhagic stroke. *Curr Neurol Neurosci Rep*. 2019;19:37.
17. Burn J, Dennis M, Bamford J, Sandercock P, Wade D, Warlow C. Epileptic seizures after a first stroke: the Oxfordshire Community Stroke Project. *BMJ*. 1997;315:1582-1587.
18. Abend NS, Beslow LA, Smith SE, et al. Seizures as a presenting symptom of acute arterial ischemic stroke in childhood. *J Pediatr*. 2011;159:479-483.
19. Cheng JH, Zhang Z, Ye Q, Ye ZS, Xia NG. Characteristics of the ischemic stroke patients whose seizures occur at stroke presentation at a single institution in Eastern China. *J Neurol Sci*. 2018;387:46-50.
20. Beniczky S, Hirsch LJ, Kaplan PW, et al. Unified EEG terminology and criteria for nonconvulsive status epilepticus. *Epilepsia*. 2013;54(suppl 6):28-29.
21. Segarra JM. Cerebral vascular disease and behavior. I. The syndrome of the mesencephalic artery (basilar artery bifurcation). *Arch Neurol*. 1970;22:408-418.
22. Castaigne P, Lhermitte F, Buge A, Escourolle R, Hauw JJ, Lyon-Caen O. Paramedian thalamic and midbrain infarcts: clinical and neuropathological study. *Ann Neurol*. 1981;10:127-148.
23. Ropper AH. “Convulsions” in basilar artery occlusion. *Neurology*. 1988;38:1500-1501.
24. Matheus MG, Castillo M. Imaging of acute bilateral paramedian thalamic and mesencephalic infarcts. *AJNR Am J Neuroradiol*. 2003;24:2005-2008.
25. Naganuma M, Hashimoto Y, Matsuura Y, Terasaki T, Hirano T, Uchino M. Two cases of top of the basilar syndrome with onset seizure [in Japanese]. *Rinsho Shinkeigaku*. 2005;45:647-651.
26. Bain SE, Hsieh DT, Vezina LG, Chang T. Bilateral paramedian thalamic and mesencephalic infarcts in a newborn due to occlusion of the artery of Percheron. *J Child Neurol*. 2009;24:219-223.
27. Gadoth A, Hallevi H. Basilar artery occlusion presenting as a tonic-clonic seizure. *Isr Med Assoc J*. 2011;13:314-315.
28. Matsuo K, Fujii C, Fuse I, Nakajima M, Takada M, Miyata K. Top of the basilar syndrome in a young adult initially presenting with a convulsive seizure. *Intern Med*. 2011;50:1425-1428.
29. Yamashiro K, Furuya T, Noda K, Urabe T, Hattori N, Okuma Y. Convulsive movements in bilateral paramedian thalamic and midbrain infarction. *Case Rep Neurol*. 2011;3:289-293.
30. Conte WL, Gill CE, Biller J. Top of the basilar syndrome presenting with convulsions. *JAMA Neurol*. 2017;74:248-249.
31. Ayas ZÖ, Kotan D. A case of first epileptic seizure diagnosed with top of the basilar syndrome. *J Neurol Stroke*. 2017;7:00244.

32. Tanaka T, Ihara M. Post-stroke epilepsy. *Neurochem Int*. 2017;107:219-228.
33. Hartings JA, Williams AJ, Tortella FC. Occurrence of nonconvulsive seizures, periodic epileptiform discharges, and intermittent rhythmic delta activity in rat focal ischemia. *Exp Neurol*. 2003;179:139-149.
34. Karhunen H, Nissinen J, Sivenius J, Jolkkonen J, Pitkänen A. A long-term video-EEG and behavioral follow-up after endothelin-1 induced middle cerebral artery occlusion in rats. *Epilepsy Res*. 2006;72:25-38.
35. Karhunen H, Bezvenyuk Z, Nissinen J, Sivenius J, Jolkkonen J, Pitkänen A. Epileptogenesis after cortical photothrombotic brain lesion in rats. *Neuroscience*. 2007;148:314-324.
36. Wu C, Wang J, Peng J, et al. Modeling early-onset post-ischemic seizures in aging mice. *Exp Neurol*. 2015;271:1-12.
37. Zhang L, Wu C, Wang J. Modeling early-onset postischemic seizures in adult and aging mice. In: NJD Wright, ed. *Basic Neurobiology Techniques*. Springer; 2020:185-212.
38. Caplan LR. "Top of the basilar" syndrome. *Neurology*. 1980; 30:72-79.
39. Saposnik G, Caplan LR. Convulsive-like movements in brainstem stroke. *Arch Neurol*. 2001;58:654-657.
40. Penfield W. Epileptic automatism and the centrencephalic integrating system. *Assoc Res Nervous Ment Dis*. 1952;30:513-528.
41. Kreindler A, Zuckermann E, Steriade M, Chimion D. Electroclinical features of convulsions induced by stimulation of brain stem. *J Neurophysiol*. 1958;21:430-436.
42. Faingold CL. The role of the brain stem in generalized epileptic seizures. *Metab Brain Dis*. 1987;2:81-112.
43. Hashizume K, Tanaka T, Fujita T, Tanaka S. Generalized seizures induced by an epileptic focus in the mesencephalic reticular formation: impact on the understanding of the generalizing mechanism. *Stereotact Funct Neurosurg*. 2000;74:153-160.
44. Browning RA. Role of the brain-stem reticular formation in tonic-clonic seizures: lesion and pharmacological studies. *Fed Proc*. 1985;44:2425-2431.