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High Doses of Caffeine-Induced Cerebral Infarction Leading to Partial Locked-In Syndrome in a Young Adult: A Novel Association?

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Keywords
Locked-in syndrome · Caffeine · Cerebrovascular incident · Hemorrhagic conversion · Brain injury

Abstract
Introduction: This is a case of a 30-year-old male with no prior medical conditions presented to the emergency department for presumed seizures after ingesting 900 mg of caffeine via pre-workout drinks and pills. ***Case Presentation:*** The patient was described as having nearly 15 min of generalized seizure activity observed by emergency medical service, requiring midazolam. A head computerized tomography (CT) demonstrated a possible thrombus, and further, CT angiography and CT perfusion confirmed a basilar artery occlusion. He was treated with tissue plasminogen activator and underwent thrombectomy achieving TICI grade 3 in the left posterior cerebral artery and TICI grade 2b in the superior cerebellar artery. Unfortunately, the patient experienced a hemorrhagic conversion leading to an incomplete locked-in syndrome. ***Conclusion:*** This case report suggests a novel association between energy drinks and caffeine supplements as potential etiologies for rapid onset on cerebrovascular incidents.

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Introduction

Locked-in syndrome (LIS) is a rare neurological condition characterized by paralysis of almost all voluntary muscles while maintaining intact cognitive functions [1]. LIS diagnosis requires understanding of neuroanatomy and the awareness of the patient's cognitive status. Current research has shown that neurobehavioral and actigraphy assessments, along with neurological imaging, can support diagnosis, but limitations still exist [1–4].

The cause of LIS often varies and is typically associated with brainstem strokes such as basilar artery or vertebral artery occlusions, traumatic brain injuries involving brainstem contusion or vertebrobasilar axis dissection, and encephalitis [1]. Chemically induced LIS mechanisms are particularly understudied, with majority of evidence derived from case reports. There have been reports of cocaine use being associated with the development of LIS [5]. Certain toxins such as curare can mimic the locked-in state [6] and highlights the need of toxicology testing for patients in which the onset of LIS has no clear trigger. Multiple substances and their interactions may play roles in causing LIS as the main or subsequent consequence, and new research efforts should be made to identify them.

The market for energy drinks and supplements is ever growing. Many contain caffeine, one of the most common psychoactive substances consumed on the planet. Controlled caffeine consumption has been associated with positive health outcomes such as reduced risk of cognitive impairment [7]; however, the specific drink or supplement with which it is consumed might have negative consequences. A growing body of research has associated consumption of energy drinks and pre-workout supplements with deleterious effects in young, healthy individuals including hypercoagulability, increased risk of ventricular arrhythmia, myocardial and cerebral infarction [8–14]. While caffeine and energy drink consumption has not been associated to LIS, patients undergoing cerebrovascular events in this context might evolve into this state. We present a 30-year-old male with no significant medical history who developed incomplete LIS after sustaining a basilar infarction associated with pre-workout drinks consumption along with caffeine pills supplements.

Case Presentation

A 30-year-old male with no past medical history presented to the emergency department for evaluation of seizure. The patient regularly drinks pre-workout drinks. The patient reportedly drank a pre-workout energy drink and consumed 400 mg caffeine pills. Per patient's medical history, two tablets of 200 mg caffeine pills were taken and initial reports of 700 mg per emergency medical service (EMS). Moments later, he told his girlfriend he had a severe headache, and she called EMS. EMS arrived and thought he was having a seizure, which reportedly lasted approximately 10–15 min, requiring midazolam for resolution. Initial blood pressure in the emergency department was 115/65, but this is most likely after the patient was sedated.

Initial computerized tomography (CT) head without contrast was completed, which showed concern for thrombus. CT angiography and CT perfusion confirmed basilar artery involvement. The patient was given tissue plasminogen activator and underwent an emergent thrombectomy. TICI grade 3 in the left posterior cerebral artery and TICI grade 2b in superior cerebellar artery were achieved.

The detailed results of the hemogram, the blood and urine biochemistry, and the basic study of hemostasis are seen below. Also listed are the results for orders placed or performed during the hospital encounter in online supplementary Table 2 (for all online suppl. material, see https://doi.org/10.1159/000538950). It is notable that the patient was positive for tetrahydrocannabinol.

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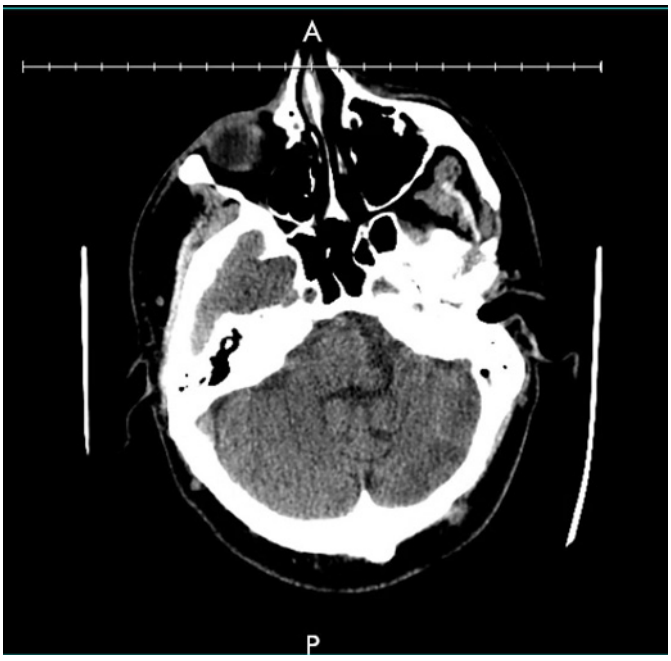

Fig. 1. Non-contrast CT scan of the head revealing left cerebellar infarct and pons. No acute intracranial hemorrhage.

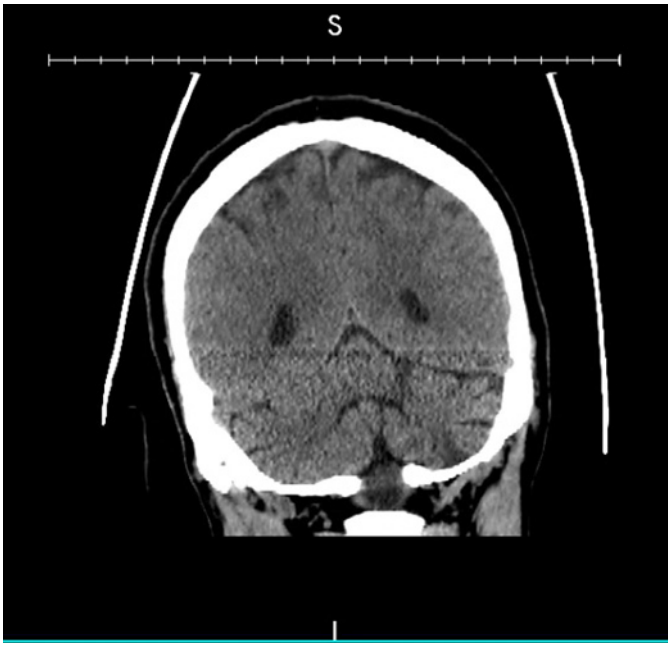

Fig. 2. Non-contrast CT scan of the head revealing left cerebellar infarct and pons. No acute intracranial hemorrhage.

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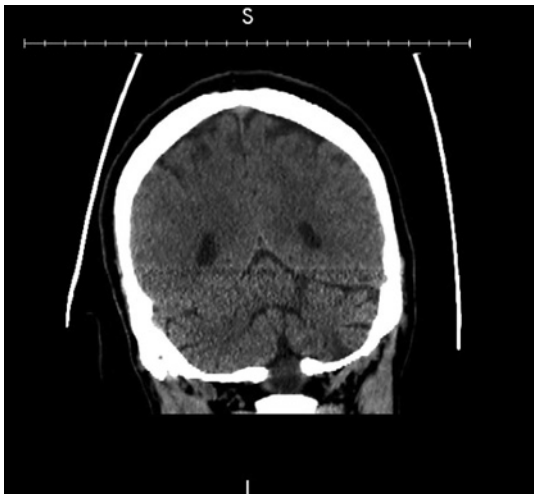

Fig. 3. Non-contrast CT scan of the head revealing left cerebellar infarct and pons. No acute intracranial hemorrhage.

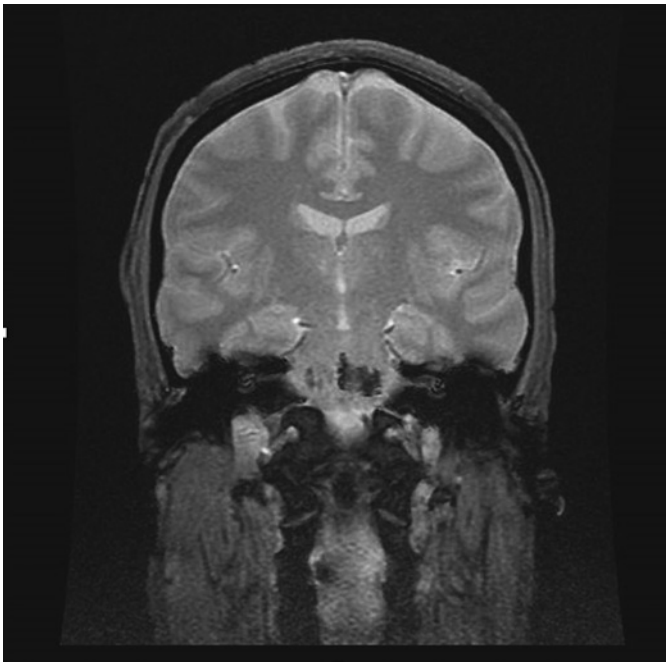

Fig. 4. His initial magnetic resonance imaging (MRI) of the brain revealed an acute infarction of the left pons.

The patient's clinical course was further complicated by cerebral edema and unfortunately, the patient developed hemorrhagic conversion. Overall, 19 days had elapsed from hospital admission to the detection of hemorrhagic transformation. The patient was on dual antiplatelet intake for 15 days. We hypothesize that hemorrhagic conversion may have occurred after mechanical thrombectomy, but the cause is idiopathic. Upon a careful review of the patient's medical record, the hemorrhagic conversion could have been caused by a prolonged usage of dual antiplatelet therapy; caffeine would play no role in this context. Additionally, it is not possible to rule out that surgical intervention contributing to hemorrhagic conversion. It is important to note that during his stroke work-up, he was found to

have a patent foramen ovale, which was surgically repaired. The patient was also evaluated for rare causes of stroke (e.g., coagulopathy, vasculitis, and Fabry disease) and these were all negative.

The patient subsequently was admitted to an acute inpatient rehabilitation center for a comprehensive brain injury rehabilitation program with left ischemic cerebellar infarct due to basilar artery thrombus status post-tissue plasminogen activator and thrombectomy. He also underwent a bilateral deep vein thrombosis duplex scan of his lower extremity, which was negative. Non-contrast CT scans of the patient's head were taken upon admission to the rehab unit showing a left cerebellar infarct and other areas of old infarcts (Fig. 1–3). His initial magnetic resonance imaging of the brain revealed an acute infarction of the left pons (Fig. 4).

Discussion

An ever-growing body of research has associated consumption of energy drinks and pre-workout supplements with negative side effects [9–14], including cerebrovascular events, which are also associated with LIS. This case is however the first to our knowledge to evolve to an incomplete LIS in the context of energy drink consumption concomitant with caffeine supplementation.

There have been several reports suggesting that energy drinks with significant increases in coagulation, platelet aggregation, arterial pressure, and decreased endothelial function in healthy individuals [9, 10]. While the mechanisms by which energy drinks might increase thrombosis and cardiovascular events risk are unknown, a prior study has proposed that energy drinks may promote platelet aggregation though arachidonic acid-induced pathways and production of prothrombotic agents [10]. The studies in which these associations were observed do not provide a conclusive result in the severity of the effect or their clinical relevance; however, these results suggest that energy drinks may increase adverse coronary or cerebrovascular events on individuals at risk [11].

Majority of case reports associate coronary events after consuming energy drinks [12]; however, there are a few reporting cerebrovascular diseases. Please refer to online supplementary Table 1 for studies involving cerebrovascular diseases after consumption of energy drinks. One of such cases involved a patient without medical history, who had a bilateral cerebellar hemorrhagic stroke after consuming energy drinks [13]. In this case, the authors cited beta-phenethylamine and other active components that might be associated with negative outcomes, including caffeine. Another case reported ischemic stroke after consumption of alcohol and large quantities of energy drinks [14]; however, the specific compound or mechanism is not suggested by the authors. Hematological disorders account for about 1.3% of all causes of acute stroke [15]. In our specific case, the brand, composition, or a particular compound in the pre-workout drink used by the patient other than caffeine could not be determined.

While sharing features with the cited cases, our case is particularly interesting as it adds another possible etiology for stroke as the patient consumed high doses of caffeine. Caffeine has been associated with positive health outcomes by many studies on coffee drinking habits, including reducing the risk for DVT [11]. However, we speculate that the caffeine in addition to energy drinks may be relevant in explaining how they may aid the suggested prothrombotic effect observed in the literature. Common energy drinks include Celsius and C4, which contains 200 mg, Monster and Rockstar, which contains 160 mg, Red Bull, which contains 80 mg, and Bang, which contains 300 mg [16]. For context, an Italian espresso shot contains an average amount of 150 mg caffeine. Common energy

drink ingredients such as taurine, synephrine [17], and other substances may also exacerbate the risk of cerebrovascular events [9–12] and therefore the risk of developing LIS. The FDA recommends no more than 400 mg caffeine in a day [18]. Even if a potential mechanism or compound cannot be pinpointed, this case continues to support that the consumption of energy drinks may have devastating cardiovascular consequences.

Our case highlights how energy drink consumption is concomitant with caffeine supplementation with cerebrovascular events. However, further research is needed to ascertain the mechanisms by which energy drinks and/or high dose caffeine consumption can lead to strokes. We recognize these limitations, but we believe the stroke to be caused by the high dose of caffeine consumed by the patient. We do not have multiple CT scans but only the CT scan upon admission to the rehab unit. The CARE Checklist has been completed by the authors for this case report, attached as online supplementary material.

Statement of Ethics

This manuscript adheres to the applicable Enhancing the Quality and Transparency Of Health Research guideline. Health Insurance Portability and Accountability Act authorization has been obtained from the patient and his surrogate for the publication of this case report. Ethical approval is not required for this study in accordance with local or national guidelines. This retrospective review of patient data did not require ethical approval in accordance with local/national guidelines. Patient informed consent was obtained for this manuscript and parents agreed in the publication of this study. Written informed consent was obtained from the patient for publication of the details of their medical case and any accompanying images.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Vijay Sinha, Loc Lam, and Michael V. Nguyen helped write the abstract, introduction, case description, and discussion.

Data Availability Statement

All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author.

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