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Case Report

Case report: Delayed posttraumatic cortical laminar necrosis secondary to spreading depolarization induced spreading ischemia from old subarachnoid hemorrhage ☆,☆☆

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ABSTRACT

Cortical laminar necrosis usually occurs secondary to infarcts or hypoxia, however other causes, including hypoglycemia, status epilepticus and immunosuppressive therapy have been reported. To our knowledge, CLN is not a phenomenon expected in the case of trauma. We report a unique case of delayed post-traumatic CLN which occurred 30 days after the initial trauma, without any proven cause apart from possible spreading depolarization induced spreading ischemia from adjacent subarachnoid hemorrhage with distinct radiologic features.

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Introduction

Cortical laminar necrosis (CLN) refers to ischemic injury of selective neuronal cortical layers due to hypoxic injury [1,2]. Usually, it occurs secondary to infarcts or hypoxia, however

other causes, including hypoglycemia, status epilepticus, and immunosuppressive therapy have been described [3]. In the chronic phase, CLN is characterized by T1-hyperintensity following the gyri of the cerebral cortex without the involvement

Abbreviations: CLN, Cortical laminar necrosis; SAH, Subarachnoid Hemorrhage; SD, Spreading depolarizations, CTA, Computerized Tomography Angiography.

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of the underlying white matter (WM) and atrophy of the cortical structures on T1-weighted MRI images [4].

While post-traumatic subarachnoid hemorrhage (SAH) and associated infarcts secondary to angiographic vasospasm may occur, blast-related vasospasm has been reported without obvious SAH [5,6]. To our knowledge, CLN is not a phenomenon expected in a posttraumatic setting and there is only a single case report that describes posttraumatic CLN without any explainable cause [7]. Here, we present an interesting case of delayed posttraumatic CLN without any proven cause apart from possible spreading depolarization (SD) induced spreading ischemia secondary to adjacent SAH with distinct radiologic features.

Case presentation

A 56-year-old gentleman was found down after an unwitnessed motorcycle accident. He was intubated in the field and brought to an outside hospital. Blood pressure was 153 of 100, pulse was 100, and oxygen saturation was over 90%. Per the outside report, the patient was awake, alert, able to open his eyes with stimulation, and moving all extremities without following commands at the initial presentation. Past medical history revealed chronic hyperlipidemia and hypertension treated with Metoprolol, Sildenafil, Atorvastatin and Furosemide. Initial unenhanced head CT showed a right parietal scalp hematoma, contrecoup hemorrhagic contusion in the left inferior temporal lobe with scattered minimal SAH and small amount of left subdural hemorrhage (SDH). CT also revealed a right sided temporal bone fracture communicating with the cranial vault and external auditory canal, resulting in possible cerebrospinal fluid (CSF) leakage from the right ear (Fig. 1). Same-day cranial MRI displayed similar findings with additional small focus of subcortical microhemorrhage in the right subcortical parietal convexity with no widespread susceptibility artifact or diffusion restriction to suggest diffuse axonal injury or fat emboli. There was no diffusion restriction or cortical swelling to suggest an infarct, seizure focus or PRES.

Follow-up CT on day-12 showed SAH washout, mostly resolved SDH and decreased size of hemorrhagic temporal contusion with no new findings (Fig. 1). Due to persistent leakage through the ear, the patient was transferred to our university hospital. 3-day video EEG monitoring was performed on days 13-15, which showed a generalized slowing which was more pronounced in the left hemisphere. Findings were consistent with moderate encephalopathy and left hemisphere finding was attributed to left temporal contusion. No seizure was captured by EEG and clinically no seizure was observed.

On day-25, a repeat head CT was obtained for hypertension, increased agitation and tachycardia to evaluate for possible new or worsening intracranial hemorrhage. However, there was no new finding with continued evolution of prior findings (Fig. 1). At this time, a lumbar puncture was performed to rule out an infectious process, which revealed normal CSF analysis and cultures. Regardless, the patient was started on empiric antibiotic treatment due to the presence of possible CSF leakage. Regarding the CSF leakage, beta-2 transferrin was nega-

tive on fluid from ear while lumbar drain was in and since removal of lumbar drain on day-15, no otorrhea was seen.

On day-30, the patient developed new aphasia with restlessness and agitation. Patient was demonstrating a high consistency following commands, with occasional single logical words spoken. This led to a CT on day-32, which showed new grey WM differentiation loss in left MCA territory within the left angular gyrus and areas of focal gyral hyperdensity in the left parietal lobe. Immediate CT-angiography was unremarkable with no evidence of vascular occlusion, dissection or focal narrowing to demonstrate angiographic vasospasm (Fig. 2).

Brain MRI obtained day-35 demonstrated gyriform cortical T1/T2-hyperintensities with no appreciable diffusion restriction involving the left parietal lobe and left posterior temporal regions including angular and supramarginal gyri, explaining patient's mixed type aphasia. On SWI, the adjacent sulci were demonstrating extensive hemosiderin staining likely from residual blood products from prior trauma, but these were not visible on most recent CT. Associated gyri and sulci were also demonstrating T2-hyperintensity on FLAIR, likely secondary to a combination of CLN and underlying blood products (Fig. 3). In the post contrast series, the intrinsic T1-hyperintensity of the affected gyri was more pronounced likely from disruption of the blood brain barrier in these corresponding regions (Fig. 4). The underlying WM was relatively well preserved on MRI and the involved parenchyma was not typical for MCA territory infarct. On DWI, there was minimal increased signal in these corresponding gyri although no signal decrease was appreciated on the ADC map. Minimal chronic SDH was also seen overlying the left ventral frontal lobe. Regarding the known contusion in the left inferior and ventral temporal lobe, this was much smaller compared with prior imaging and markedly distant than the above-mentioned regions.

Patient's admission was quite prolonged and was not able to be discharged until day-53. Hospital course was complicated by requirement of PEG tube for feeding, significant agitation, as well as development of otomastoiditis requiring IV antibiotics. Otomastoiditis was noted on MRI as well and was a likely source of recurrent fevers throughout his hospitalization, which eventually improved with a 2-week intravenous antibiotic course. Patient eventually stabilized without fevers and with improvement, although agitation didn't resolve. Patient has not followed-up at the time of this writing 5-weeks after discharge to determine clinical improvement.

Discussion

Here, we present an interesting case of CLN, which developed on imaging 32 days after trauma. While CLN is commonly seen with hypoxic injury, cardiac arrest, seizures, or stroke, we couldn't identify a typical source clinically or radiologically. However, we noted extensive evolving SAH, and associated hemosiderin staining entrapped in the sulci adjacent to the affected gyri, and thus we hypothesized that possible toxic irritation from the adjacent blood products might have caused findings, given the lack of any identifiable stroke,

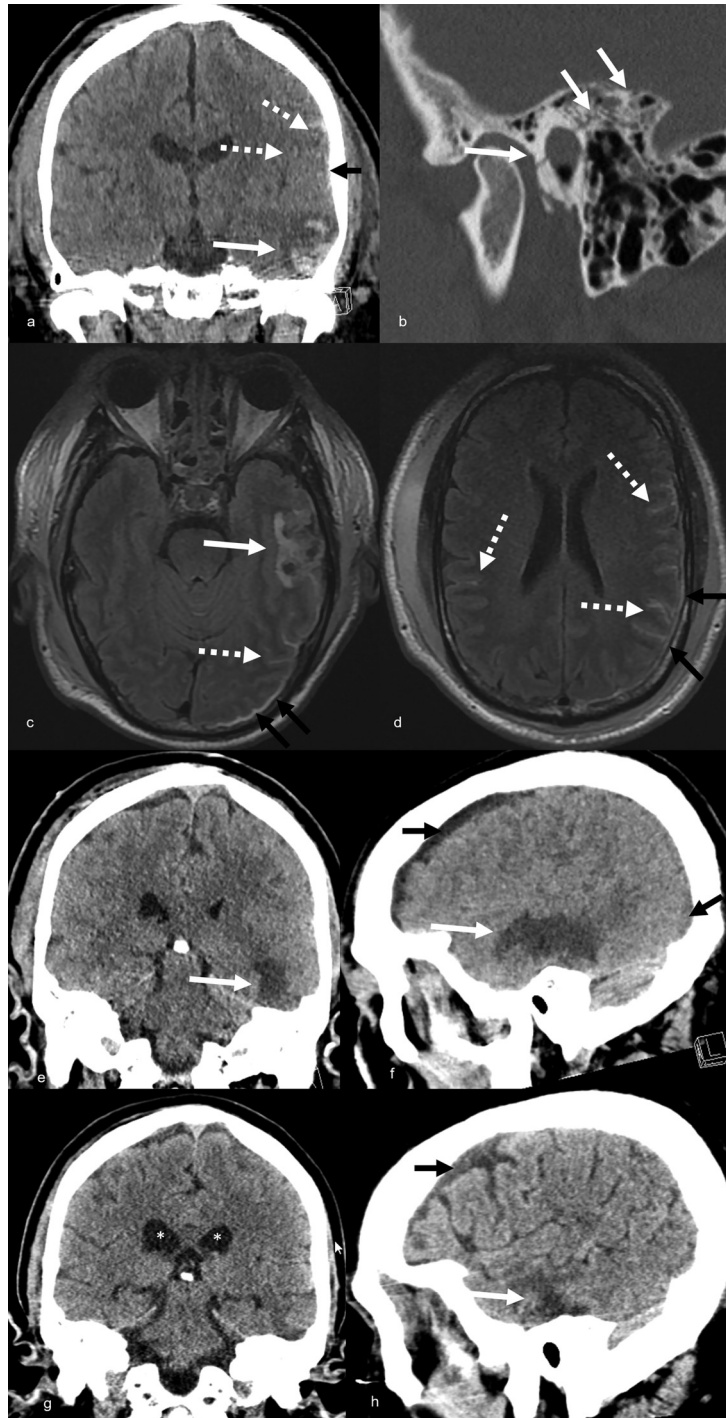


Fig 1 – (A) Non-enhanced coronal head CT in day-1, shows a counter coup hemorrhagic contusion in the left inferolateral temporal lobe (white arrow), scattered left subarachnoid hemorrhages (dotted arrow) and trace left subdural hemorrhage (black arrow). **(B)** Sagittal bone window shows an oblique fracture in the right temporal bone connecting the cranial vault with the right external auditory canal due to coup injury (white arrows). **(C-D)** Axial T2-FLAIR brain MRI obtained at the same day shows similar findings, trace subdural hemorrhage overlying the left cerebral hemisphere (black arrows), scattered wide spread subarachnoid hemorrhages in the left, but also in a lesser degree on the right (dotted arrows) and left ventrolateral hemorrhagic contusion. **(E-F)** Non-enhanced CT in axial and sagittal view in day-12. Hemorrhagic contusion is evolving (white arrows). Prior subarachnoid hemorrhage is no longer visible. Trace chronic subdural collection is present overlying the left frontal and occipital lobe, may represent hygroma, chronic subdural hemorrhage or from intracranial hypotension. **(g-h)** Non-enhanced CT in axial and sagittal view in day-25. Hemorrhagic contusion is mostly healed (white arrow). No subarachnoid hemorrhage is present. Subdural collection is barely visible (black arrow). However, patient's lateral ventricles are slightly larger than before, raising question for developing hydrocephalus (*).

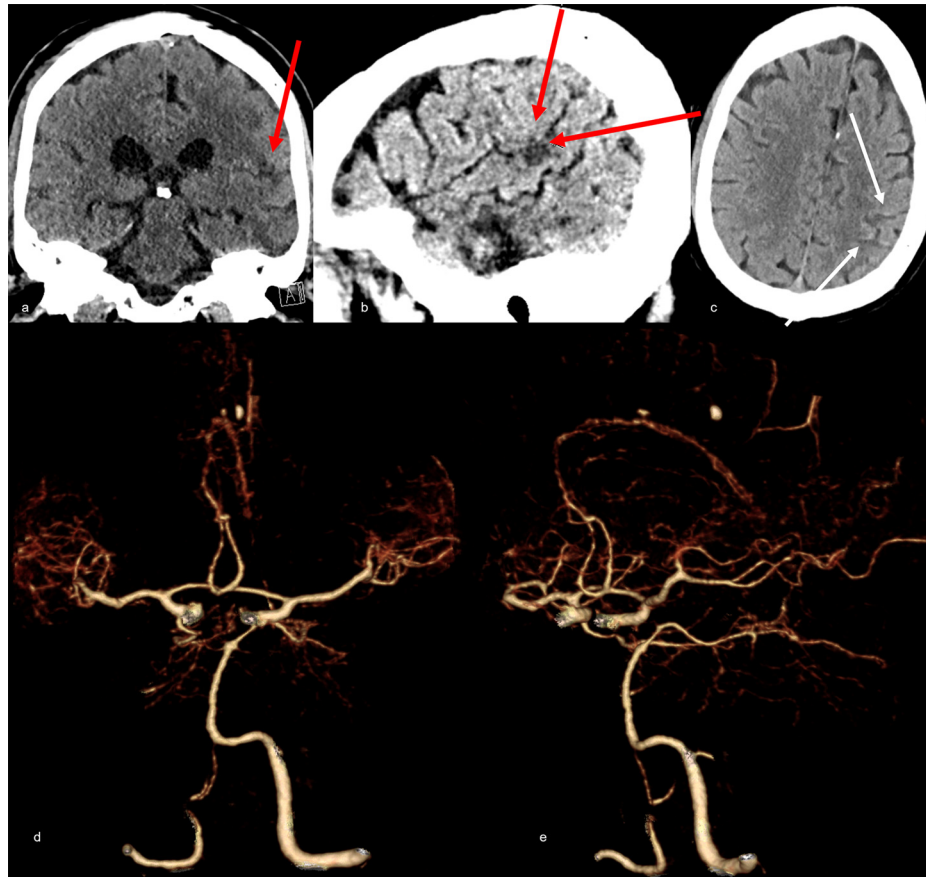


Fig. 2 – Non-enhanced head CT in day-32 in coronal (A), sagittal (B) and axial (C) plane. Again, ventricles are slightly prominent without any midline shift or worsening hydrocephalus. However, there is new loss of grey-white matter differentiation in the left angular gyrus (red arrows). At a higher level in the left parietal, there is relatively hyperdense appearance of gyri with heterogeneous appearance of the adjacent sulci (white arrows). Same day volumetric CT-angiography (D) coronal view and (E) oblique left view, did not show any stenosis or occlusion in the associated vasculature.

seizure, hypoxia, cardiac arrest, and angiographic vasospasm. This phenomenon was noted by Dreier et al. in 1998 when they demonstrated in animal studies that, products of hemolysis such as hemoglobin and potassium in the subarachnoid space caused spreading depolarization in the adjacent tissues and this lead to spreading ischemia which gives rise to cortical laminar necrosis [11,12]. Our radiologic findings demonstrate similarity to pathologic specimens with cortical infarcts obtained from the rats in the experiment by Dreier et al. [12]. There is a plethora of evidence that suggests that territorial infarction can occur in the regions dependent on the affected arterial structures secondary to angiographic vasospasm in the setting of SAH from ruptured aneurysms, usually expected in 3-5 days, lasting up to 2-3 weeks. Posttraumatic SAH and associated angiographic vasospasm has been reported, starting within 1-2 days with a peak at the first week [6]. Associated infarcts usually include a larger vascular territory from the affected branches with involvement of the underlying WM. On the other hand, delayed ischemic cortical lesions may still occur in the absence of angiographic vasospasm in patients recovering from aneurysmal SAH in the cortical regions adjacent to the aneurysmal rupture [8,9]. Hartings et al. hypoth-

esized that cortical exposure to subarachnoid blood products gave rise to long-lasting SD which in turn induced ischemia of small cortical arteries, resulting in CLN in adjacent structures [10]. The authors injected blood in the sulci to mimic SAH in swine models and they were able to show focal CLN adjacent to subarachnoid clots on histopathology. They were able to detect SD with electrocorticography in corresponding regions. For that reason, authors recommended monitoring SD subsequent to SAH with electrocorticography, and not simply rely on assessment of angiographic vasospasm to rule out the risk of delayed cortical infarcts.

There are simply 3 types of vasospasm which can occur after subarachnoid space, proximal angiographic vasospasm, sustained vasospasm in the microcirculation, and vasospasm in the microcirculation leading to spreading ischemia triggered by SD. SD induced vasospasm in the microcirculation actually can be physiologic in order to sustain the brain perfusion with alterations in arterial resistance, causing predominant hyper perfusion followed by a mild oligemia in normal tissues [13]. In other cases, this response could be more severe or prolonged with resultant hypoperfusion and spreading ischemia [11,12,14].

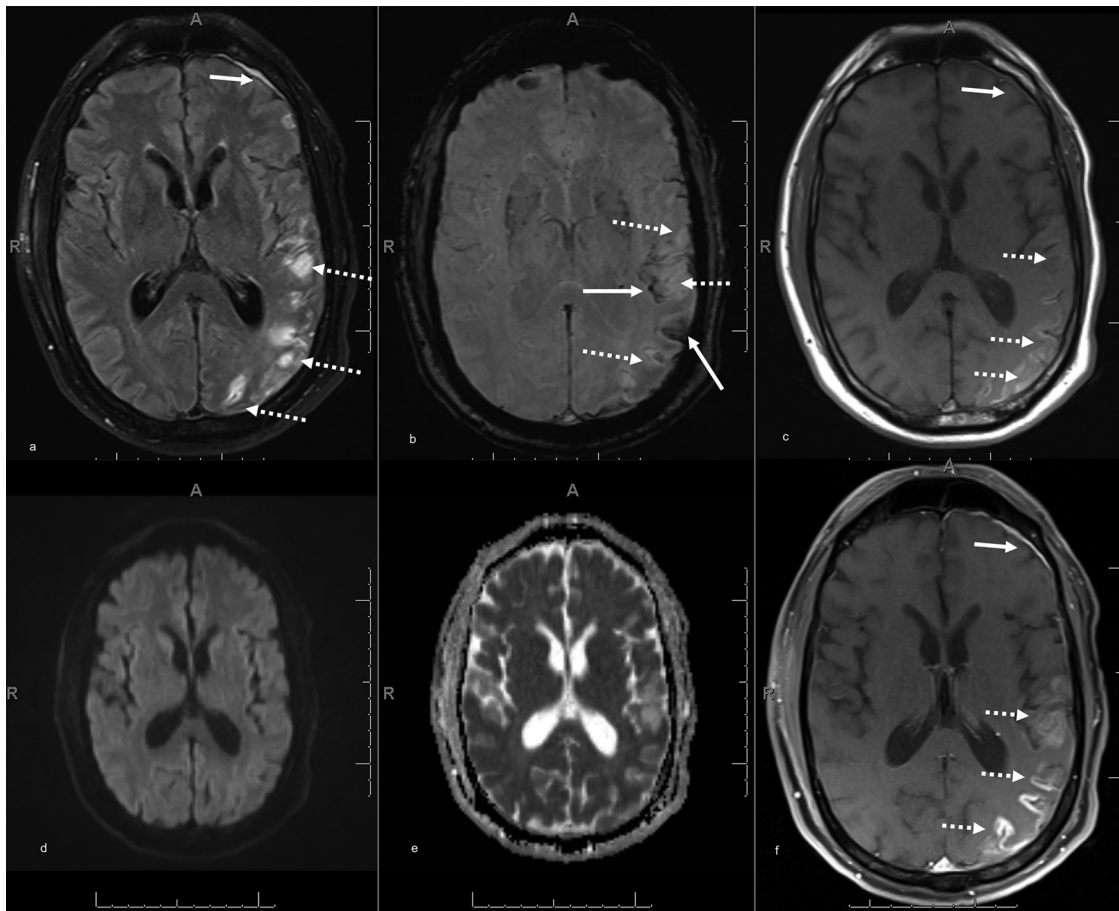


Fig. 3 – Contrast enhanced MRI of the brain on day-35. (A) Axial fat saturated T2-FLAIR, shows abnormal cortical and sulcal signal(dotted arrows) in the left temporo-parieto-occipital region. Subdural effusion vs thickening overlying the left frontal lobe (arrow). (B) Axial SWI shows dark hemosiderin products in the sulci (arrow) and T2 hyperintense signal in the adjacent cortices (dotted arrow). (C) Non enhanced axial T1 series show T1 hyperintensity in the effected gyri (dotted arrows). As seen on trace image (D) and ADC map (E), there is no corresponding diffusion restriction in these areas. (F) Post contrast axial fat saturated T1 image shows increased conspicuity of the T1 hyperintense gyri secondary to blood brain barrier loss, consistent with cortical laminar necrosis (dotted arrows). The subdural collection overlying the left frontal lobe is diffusely enhancing (arrow), compatible with pachymeningeal enhancement, likely from intracranial hypotension.

Our clinical and radiologic findings in this case fit with the findings of Hartings et al. and supports their hypothesis in real human clinical setting. Our patient's findings were highly unusual for an infarct secondary to angiographic vasospasm, given the presence of normal CT-angiogram, the preservation of the adjacent WM, scattered sparing of few cortical structures unlike a typical vascular territorial infarct and normal diffusion weighted imaging findings. As described above, local subarachnoid blood products may cause SD which leads to spreading ischemia in the adjacent vulnerable cortical neurons as suggested. To our knowledge, the only known case of similar phenomenon was reported by Schinke et. al. in 2018 (3). Compared with their case and imaging examples, the distribution of CLN is more distinctive and more extensive in our case report with more supportive evidence.

Our study is limited by the fact that we only have 1 vascular imaging method, a CT-angiography which was obtained

at day-32. While a digital subtraction angiography is known to be the most sensitive modality to identify subtle detection of vasospasm, it is an invasive method with potential complications, thus digital subtraction angiography was not employed in our patient. Unfortunately, we didn't obtain any vasculature imaging prior, due to the fact that the patient was clinically and radiologically improving. It is possible that the patient might have developed angiographic vasospasm that we missed during the initial 32 days. However, the likelihood is significantly low, due to the preservation of the adjacent WM. While angiographic vasospasm is an important factor in the development of delayed cerebral ischemia, in a large meta-analysis based on data in several thousand patients by Etminan et al. demonstrated a dissociation between radiographic vasospasm and clinical outcome, and the worse outcome could be attributed to delayed cerebral ischemia from SD induced spreading ischemia [15]. Considering all of

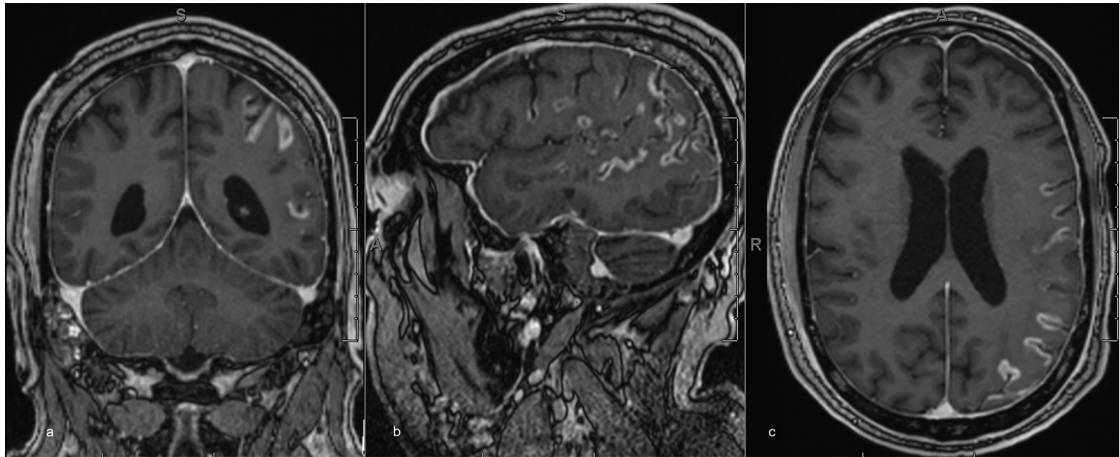


Fig. 4 – Contrast enhanced coronal (A), sagittal (B) and axial (C) MPRAGE sequence of the brain on day-35 is better demonstrating the affected gyri with cortical laminar necrosis with relative sparing of some adjacent cortical structures in the same location and normal looking adjacent subcortical white matter, in a fashion not expected in the setting of a MCA territory infarct of this size. Pachymeningeal enhancement could be from intracranial hypotension, better seen in this view.

these features, we hypothesized that pooled subarachnoid chronic blood products were producing SD, which induced local vasospasm in the microcirculation and caused spreading ischemia in a highly delayed phase after the initial trauma.

Conclusion

A rare case of posttraumatic delayed CLN is presented without any possible underlying explanation such as hypoxia, cardiac arrest, seizure, infection, hypoglycemia or large vessel occlusion. The only viable explanation is that posttraumatic SAH was present in the effected regions, this likely resulted in SD induced spreading ischemia which gave rise to the development of CLN. This observation can be tested with larger case series in the future and could be a resource for radiologists and clinicians who would encounter a similar picture late in the post-traumatic setting.

Patient consent

The author was unable to obtain written consent from the patient or from the patient's relatives, despite attempts to do so. Because of the public interest in publication, the anonymization of the patient, and that attempts had been made to contact the patient and their relatives, exceptional agreement for publication of the case report was given by the Editor-in-Chief of the journal *Radiology Case Reports*.

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