Case Report: Fluctuating mental status and new paradoxical left hemispatial neglect during inpatient rehabilitation for left temporo-occipital intracerebral hemorrhage with

intraventricular hemorrhage

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Competing interests: The authors have neither any competing interests nor any funding, grants, or financial benefits to disclose. The authors of this manuscript, Justin Weppner, Jenna Meriggi, and Kevin Franzese have nothing to disclose. No funding was received for this study.

In training statement: Justin Weppner and Jenna Meriggi are in training at the time of manuscript submission.

Previous publication or presentation: This case was submitted in abstract form to the Association of Academic Physiatrists 2020 annual meeting.

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Key words: cerebral vasospasm, intraventricular hemorrhage, intracerebral hemorrhage, brain injury medicine

Brief history and physical exam

A 61-year-old man with a past medical history significant for an automatic implantable cardioverter-defibrillator (AICD) placement for a left bundle branch block and Budd Chiari syndrome of unknown etiology (on chronic warfarin therapy) was admitted to the inpatient rehabilitation unit, following a spontaneous left temporo-occipital intracerebral hemorrhage (ICH) with intraventricular hemorrhage (IVH) secondary to supra-therapeutic international normalized ratio (INR) of 4 (goal: 2–3) (Figure 1). Warfarin was reversed with fresh frozen plasma and vitamin K and an external ventricular drain (EVD) was placed. On acute hospital day (HD) 2, he underwent digital subtraction angiography, which revealed no aneurysm or vascular anomaly to explain the bleeding and no cerebral vasospasm. The 13-day acute hospital course was complicated by delirium, ileus, hyponatremia, and difficulty weaning off the EVD. The EVD was removed on acute HD 12; he was then monitored for 24 h before transferring to the inpatient rehabilitation unit for comprehensive rehabilitation.

During admission at the rehabilitation unit, the patient's vital signs were stable, and he was alert and oriented to self, place, and year. He was able to follow simple commands, his cranial nerves II–XII were grossly intact, he had full muscle strength of the bilateral upper and lower extremities, and he demonstrated no visuospatial neglect with no extinction on double simultaneous stimulation. To further assess for visuospatial neglect a cancellation task was performed during initial the therapy evaluation in which the patient had to find and cancel target items that were distributed on an A4-sized sheet of paper. Medications included daily doses of aspirin (81 mg), atorvastatin (40 mg), enoxaparin (40 mg), lisinopril (10 mg), and melatonin (3 mg) at night.

On inpatient rehabilitation HD 3, during the team's interdisciplinary conference, the therapy team noted that he exhibited a new paradoxical left hemispatial neglect, which did not anatomically correspond with the diagnosis of left ICH with IVH. He was reassessed, and his vital signs were unremarkable. On physical examination, he appeared drowsy and required verbal and tactile stimulation by the examiner to stay awake. He was oriented to person only, which was a decline from his orientation to person, place, and year earlier that same morning. Moreover, he demonstrated difficulty following simple commands without mimicking. A new left hemispatial neglect was noted on the double simultaneous stimulation with right gaze preference. The patient was not able to participate in manual muscle testing or cranial nerve examination. This case study conforms to all CARE guidelines and reports the required information accordingly (see Supplementary Checklist, Supplemental Digital Content, http://links.lww.com/PHM/A863).

In summary, our patient with a history of left ICH with IVH now presented with fluctuating mental status, a new paradoxical left hemispatial neglect, and right gaze preference. What is the differential diagnosis for this patient?

Differential diagnosis

The list of differential diagnoses for a patient with new neurologic impairment and decline in mental status would first include worsening of ICH, transient ischemic attack, acute ischemic stroke, or new intracranial hemorrhage. To evaluate for these abnormalities, a non-contrast computed tomography (CT) scan of the brain can be performed to evaluate for worsening of ICH or acute intracranial bleeding. The ventricles can also be assessed by a non-

contrast head CT scan to evaluate for hydrocephalus. If the non-contrast head CT scan does not reveal any acute abnormalities, it may be followed by a CT angiogram to evaluate for cerebral vasospasm or vascular abnormality, and a magnetic resonance imaging (MRI) scan of the brain to evaluate for acute ischemic stroke, which may not appear on a non-contrast CT scan. If the MRI scan is contraindicated, a CT perfusion scan may be utilized instead to assess for ischemia.

While awaiting imaging, additional evaluations and testing should be considered. Side effects of medications could potentially cause mental status changes, and new or sedating medications should be reviewed and considered as potential causes. Vital signs including pulse oximetry can also provide valuable information when considering the differential diagnosis, as hypoxia could potentially cause an altered mental status. Temperature, heart rate, and respiratory rate combined with a complete blood count may assist in identifying potential infectious complications such as sepsis, encephalitis, meningitis, and meningoencephalitis. A point-of-care glucose test may be conducted quickly at the bedside to assess for hypo or hyperglycemia. Additional laboratory evaluations may be ordered to assess for electrolyte abnormalities such as hypernatremia, hypocalcemia, hyponatremia, acute kidney failure. uremia. and hyperammonemia.

Seizure activity may result in an altered mental status, and a spot electroencephalogram (EEG) may be performed to evaluate for seizures. If the diagnostic evaluations are uninformative with no acute abnormalities on brain imaging, a lumbar puncture could be considered for a complete evaluation for meningitis and hydrocephalus. Diagnoses of exclusion such as

pseudoseizure, conversion disorder, psychosis, and delirium should be considered only when other diagnoses are ruled out (Table 1).

Given the differential diagnosis, what laboratory tests or radiologic imaging should be ordered for further evaluation?

Diagnosis and discussion of management and outcome

The patient's medication was reviewed. He had no new medications or sedatives. A point-of-care glucose test revealed normal blood glucose levels. As previously mentioned, the brain MRI was contraindicated in the setting of AICD.

A non-contrast head CT scan was ordered to evaluate the progression or worsening of ICH. CT angiography was ordered to evaluate vascular abnormalities. Finally, a CT perfusion scan was ordered to assess for ischemia. Unfortunately, five critically ill trauma patients were queued for CT scans, and therefore a CT machine was not available for approximately 50 minutes. In the meantime, labs were drawn including a CBC, CMP, serum ammonia, and coagulopathy panel, and the patient was escorted for an EEG. A spot EEG showed a well-developed, symmetric, rhythmical 8–9 Hz posterior dominant rhythm that attenuated with eye opening. The background was continuous, spontaneously variable, and appropriately reactive. EEGs while the patient was awake and asleep showed no evidence of epileptiform discharges, seizures, or focal abnormalities.

Following the EEG, the CT machine became available, and the patient was escorted directly to the radiology department. Non-contrast head CT was performed to evaluate the progression or worsening of ICH, followed by CT angiography to evaluate for vascular abnormality and a CT perfusion scan to assess for ischemia. Non-contrast head CT revealed maturing subacute left temporo-occipital ICH with no new interval hemorrhage or acute infarct (Figure 1). Ventricles were stable in size without signs of hydrocephalus. The CT angiogram revealed diminutive supraclinoid internal carotid arteries and carotid termini with relative diminutive caliber of the bilateral proximal A1 and M1 segments, which was consistent with a cerebral vasospasm. CT perfusion showed reduced cerebral volume corresponding to the recent left ICH with no additional areas of conspicuous asymmetry on perfusion maps. The time from initial evaluation for decline to diagnosis of cerebral vasospasm was approximately 121 minutes. A physician escorted the patent to the EEG lab and radiology, and upon physical examination, the patient remained stable with no further decline noted on serial examinations.

The labs that were ordered revealed normal sodium, potassium, chloride, blood urea nitrogen, creatinine, calcium, alanine aminotransferase, aspartate amino transferase, and serum ammonia levels. With normal serum ammonia and liver function tests, symptomatic Budd Chiari syndrome was unlikely to be the cause of his symptoms. He did not have coagulopathy that could worsen ICH with a prothrombin time of 14.2 seconds, INR of 1.1, and platelet count of 182×10^9 /L. His white blood cell count was unremarkable, and together with normal vital signs, an infectious process was unlikely.

Considering these imaging findings, what specialty referrals would you make and how would you manage this patient?

Neurosurgery was consulted for angiography, and the neurology stroke service was consulted for post-procedure care and management. He was transferred back to acute care for subsequent digital subtraction angiography, which revealed a severe flow-limiting vasospasm of the bilateral internal carotid arteries and bilateral A1 and M1 segments that was worse on the right side when compared to the left side. He received intra-luminal verapamil injected through the angiography catheter directed at the vasospasm followed by placement of an EVD, which improved his mental status and resolved the left-sided neglect. He was transitioned to oral nimodipine for vasospasm treatment and prevention. The EVD was removed on acute readmission HD 5, and he returned to inpatient rehabilitation after a week of acute care management and cerebral vasospasm monitoring. Subsequently, he was discharged to a skilled nursing facility for continued rehabilitation, and eventually discharged home at a modified independent level of function.

What can we learn from the diagnosis, treatment, and management of this patient?

This was a case of fluctuating mental status, a new paradoxical left hemispatial neglect, and right gaze preference in an ICH patient with IVH. The severe flow-limiting vasospasm of the internal carotid arteries and A1 and M1 segments caused reversible cerebral ischemia, thereby leading to left hemispatial neglect. The hemispatial neglect was contralateral to the damaged hemisphere, and the left temporo-occipital intracerebral hemorrhage that the patient presented with to rehabilitation would not explain his new symptoms. Once the treatment team reported findings of left hemispatial neglect with discordant radiologic imaging of left-sided ICH, a wide differential diagnosis was considered. Additional imaging and laboratory evaluations were conducted, identifying a cerebral vasospasm that could have resulted in bilateral irreversible cerebral ischemia. A team approach is the hallmark of rehabilitation, and interdisciplinary teams emphasize open, honest, and direct communication, helping advance safe and effective patient care. This patient's fluctuating presentation further underscores the importance of team communication as otherwise it may have dangerously progressed before a definitive diagnosis.

Neuroimaging has revolutionized healthcare; however, advanced imaging studies must be interpreted within the context of physical examination findings, and overreliance on neuroimaging should be avoided. This case demonstrates the importance of correlating physical examination findings with radiographic anatomy, and when the two findings are discordant, further investigations are necessary. Physical examination findings can make a strong case for the presence of a pathologic process, despite not being observed in the current radiologic imaging, as there are limits to each imaging technique.

ICH with IVH portends a worse prognosis and increases the 30-day mortality (43–80%) compared to ICH without IVH (9%). Increased ICH volumes can foretell poorer outcomes.^{1,2} One theory is that the extension of blood into the subarachnoid space might mirror the same pathways associated with subarachnoid hemorrhage (SAH). Cerebral vasospasm is a well-known expected complication of SAH. Clinically significant cerebral vasospasms affect 20–30% of patients with SAH.^{3,4} The principal pathophysiological mechanism is proposed to be facilitated

by circulating heme products within the cerebrospinal fluid; thus, ICH patients with IVH may also be at risk for developing cerebral vasospasms.³ While the true incidence of cerebral vasospasm secondary to ICH with IVH has not been well-described, a study on 115 patients with ICH reported an incidence of 5.6%.⁵ In the setting of SAH, vasospasm usually occurs at HD 3–14, with a peak incidence at approximately 7 days after the original event.⁶ In the present case, it was unclear when the vasospasm began. It occurred sometime within the 15 days between the negative (acute HD 2) and positive (inpatient rehabilitation HD 3) angiograms, and if the cerebral vasospasm occurred on inpatient rehabilitation HD 3, he would have been outside the expected window for a cerebral vasospasm, since vasospasm was not be expected in this timeframe during acute rehabilitation.

EVD placement has a protective effect against the development of cerebral vasospasms, with a three-fold decreased incidence in SAH patients with an EVD.⁷ We hypothesized that the protective nature of the EVD, which helps to eliminate subarachnoid blood and heme products, may have delayed the onset of the cerebral vasospasm in this patient until 3 days post-EVD removal.

When physical examination findings are conflicting with the expected findings based on radiographical anatomy, further evaluation is warranted, and a broad differential diagnosis should be considered. Strong interdisciplinary teamwork is a hallmark of effective rehabilitation management and encourages all team members to feel comfortable in reporting concerns noted on therapy, while nursing evaluations are also vital. Active listening from the rehabilitation physician and addressing concerns noted by the therapy team can improve the effectiveness of medical care provided in the rehabilitation unit. While ICH is not commonly associated with cerebral vasospasm, practitioners treating patients with ICH should be aware of the risk of cerebral vasospasm associated with IVH. If a patient with ICH and IVH experiences clinical deterioration during inpatient rehabilitation, then cerebral vasospasm should be considered in the differential diagnosis.

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Figure 1

1A: Non-contrast head computed tomography (CT) on acute hospital day 1 demonstrated an intracerebral hemorrhage (ICH) centered in the posterior left temporo-occipital region (approx. 6.9×3.6 cm) with surrounding vasogenic edema.

1B: Non-contrast head CT on hospital day 1 shows the ICH with extension into the ventricular system with intraventricular hemorrhage.

1C and 1D: Non-contrast head CT on rehabilitation hospital day 3, a fortnight after initial noncontrast CT scan, demonstrates a subacute left temporo-occipital hematoma with a decreasing mass (compared to figures 1A and 1B).

Table 1

Differential diagnosis for a patient with a history of left intracerebral hemorrhage, now presenting with fluctuating mental status, new paradoxical left hemispatial neglect, and right gaze preference.

Figure 1

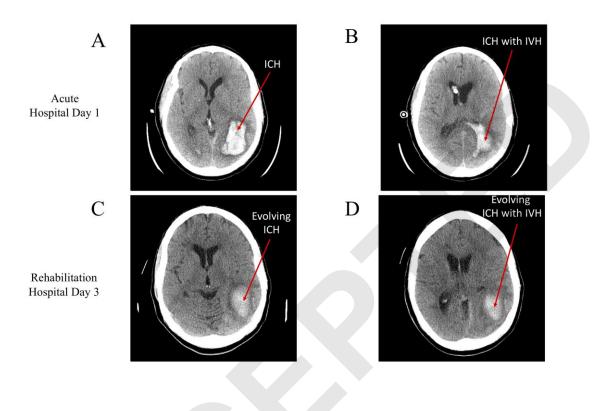


Table 1

Differential diagnosis	Manifestation or symptom
Neurologic dysfunction	Hydrocephalus
	• Transient ischemic attack Ischemic
	stroke
	• Worsening intracerebral hemorrhage
	Cerebral vasospasm
	• Seizure
Electrolyte abnormality	Hyponatremia
	Hypernatremia
	Hypocalcemia
Renal dysfunction	Acute kidney failure
	• Uremia
Hepatic dysfunction	Hyperammonemia
Endocrine dysfunction	Hypoglycemia
	Hyperosmolar hyperglycemic state
Infection	• Encephalitis
	Meningitis
	Meningoencephalitis
	• Sepsis
Pulmonary dysfunction	• Hypoxia
Psychiatric conditions	Pseudoseizure
	Conversion disorder
	Psychosis
	• Delirium
latrogenesis	• Side effects of medication