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Case Report

Cerebral microdialysis demonstrates improvements in brain metabolism with cerebrospinal fluid diversion in spontaneous intracerebral hemorrhage

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ABSTRACT

Background: Cerebral microdialysis (CMD) is an FDA-approved multimodal invasive monitoring technique that provides local brain metabolism measurements through continuous interstitial brain fluid sampling at the bedside. The past applications in traumatic brain injury and subarachnoid hemorrhage show that acute brain injury (ABI) can lead to a metabolic crisis reflected by changes in cerebral glucose, pyruvate, and lactate. However, limited literature exists on CMD in spontaneous intracerebral hemorrhage (ICH).

Case Description: A 45-year-old woman presented with a Glasgow Coma Scale of 8T and left frontal ICH with a 6 mm midline shift. She underwent craniotomy and ICH evacuation. Intraoperatively, CMD, brain tissue oxygenation ($PbtO_2$), intracranial pressure (ICP), and cerebral blood flow (CBF) catheters were placed, targeted toward the peri-hematoma region. Postoperatively, ICP was normal; however, $PbtO_2$, CBF, glucose, and lactate/pyruvate ratio were abnormal. Due to concern for the metabolic crisis, poor examination, and hydrocephalus on computed tomography of the head (CTH), she underwent external ventricular drainage (EVD). Post-EVD, all parameters normalized ($P < 0.05$ on Student's *t*-test). Monitors were removed, and she was discharged to a nursing facility with a modified Rankin scale of 4.

Conclusion: Here, we demonstrate the safe implementation of CMD in ICH and the use of CMD in tandem with $PbtO_2$/ICP/CBF to guide treatment in ICH. Despite a normal ICP, numerous cerebral metabolic derangements existed and improved after cerebrospinal fluid diversion. A normal ICP may not reflect underlying metabolic-substrate demands of the brain during ABI. CMD and $PbtO_2$/CBF monitoring augment traditional ICP monitoring in brain injury. Further prospective studies will be needed to understand further the interplay between ICP, $PbtO_2$, CBF, and CMD values in ABI.

Keywords: Brain metabolism, Brain path, Cerebral brain oxygenation, Cerebral microdialysis, Spontaneous intracerebral hemorrhage

INTRODUCTION

Cerebral microdialysis (CMD) is a well-established, FDA-approved technique of multimodal brain monitoring used to provide measurements of local brain metabolism through continuous sampling of brain interstitial fluid. A catheter is inserted into the area of interest in the brain, yielding measurements of various metabolites such as glucose, lactate, pyruvate, and a lactate to pyruvate (L/P) ratio.[19] These metabolites can also provide insight into the damage's severity or extent.[1-

3] Elevated L/P ratio (>40) has been termed a "metabolic crisis" and has been associated with poor outcomes.[20] Past studies have illustrated the promise of CMD in subarachnoid hemorrhage (SAH) to guide individualized neurocritical care, showing that CMD can help detect delayed cerebral ischemia approximately 12 h before onset. In CMD studies analyzing SAH and traumatic brain injury (TBI), abnormal L/P ratios and glucose, lactate, and pyruvate levels have been shown to indicate disturbances in brain metabolism that may predict neurological outcomes between 3 and 12 months after the onset of the acute neurological injury (ANI).[7,11,15] The merits of CMD in spontaneous intracerebral hemorrhage (sICH) are yet to be delineated.

Changes in metabolic activity relating to ICH are observed, particularly in the peri-hemorrhagic zone (PHZ), the area surrounding the point of injury or damage. Past studies on TBI and SAH have observed decreased glucose and elevated L/P from CMD catheters in the PHZ as compared to normal brain in the same patient, indicating an interruption of adequate metabolism in specific areas of the brain.[8,17] Recent CMD studies have demonstrated altered metabolic parameters in the PHZ of sICH; however, the clinical utility of this metabolic data has yet to be addressed.[13,16] Historically, invasive neuromonitoring has been guided by intracranial pressure (ICP) monitoring alone, though emerging evidence suggests ICP may not reflect the state of local tissue metabolism and autoregulation.[10] Therefore, brain tissue oxygenation ($PbtO_2$) measurements and CMD with ICP monitoring could help guide treatment paradigms for patients with sICH.

Here, we describe a case of sICH that utilized CMD in tandem with $PbtO_2$ and cerebral blood flow (CBF) monitoring to guide the initiation of external ventricular drainage (EVD) following craniotomy and minimally invasive parafascicular surgery for the evacuation of the hemorrhage.

CASE PRESENTATION

A 45-year-old female presented with slurred speech and left-sided twitching and weakness with rapid decline to becoming unresponsive. She had a past medical history of methamphetamine abuse and hypertension. Physical examination showed an intubated patient with a Glasgow Coma Score of 8T. She opened her eyes to noxious stimulation and had reactive pupils and purposeful movements of her left upper and lower extremities with minimal movements of the right upper and lower extremities. Computed tomography (CT) scans of the brain revealed an 87 cc (6.5 × 6.2 × 4.3 cm/2 using the A × B × C/2 estimation) ICH in the left frontal region (extending to the basal ganglia with intraventricular hemorrhage and effacement of the ventricles [Figures 1a and b]. She underwent subsequent craniotomy with minimally invasive evacuation of the ICH. A quad lumen bolt was placed at the time of surgery in the left frontal region, resulting in the monitor tips in the peri-hematoma zone. The post-operative CT scans of the brain showed adequate evacuation of the hematoma with a small residual hematoma [Figures 1c and d]. Following surgery, increases were observed in L/P ratios, and $PbtO_2$ was persistently below 20 mmHg. ICP remained below <22 mmHg. A right frontal ventriculostomy drain was placed to address the occult regional ICP crisis. Following placement of the drain, L/P ratios lowered toward normal thresholds, and $PbtO_2$ improved to above >20 mmHg [Figures 2 and 3]. The Hemedex CBF values also improved from values of 5–10 mL/100 g-min to the more normal range of 25–30 mL/100 g-min.[14] These monitors remained in place until all of the monitors were removed on post-operative day #5. She subsequently had a tracheostomy and percutaneous endoscopic gastrostomy, followed by weaning and removal of the ventriculostomy. She did not develop hydrocephalus [Figure 4]. She was eventually discharged to a skilled nursing facility with a Modified Rankin Scale of 4, residual aphasia, and right-sided weakness.

Operative technique and brain monitor placement

The left basal ganglia hemorrhage was approached through a minimally invasive parafascicular surgery (MIPS) approach with the BrainPath™ Cannula (Nico Corporation, Indianapolis, IN) using a trans sulcal approach along the long access of the blood clot.[9,12] The brain was decompressed based on visual inspection after the evacuation. A separate incision on the same side was made over Kocher's point, where a quad-lumen bolt was placed through a twist drill hole.[5] The four lumens of this bolt were used for the following probes: Hemedex (CBF) (Hemedex, Waltham, MA), CMD (M-Dialysis, Chelmsford, MA) catheter, brain oxygenation through Licox catheter (Integra, Princeton, NJ), and a Camino ICP (Natus, Middleton, WI) probe.

DISCUSSION

In this study, we demonstrate the evacuation of an ICH through MIPS using the BrainPath™ cannula with resultant abnormal multimodal monitor parameters despite adequate resection. Postoperatively, the patient had suboptimal lactate/pyruvate values, which correlated with low $PbtO_2$, suggesting a metabolic crisis. We demonstrate the first case of clear temporal improvement in metabolic parameters following the placement of EVD in a surgically evacuated sICH.

A striking aspect of this case is the discordance between ICP and metabolic parameters. In the Monroe-Kellie Principle, ICP is inversely affected by increased intracranial volume. High ICPs result in lower cerebral perfusion pressure (CPP) and, therefore, a state of tissue oliguria, subject to whether microcirculatory autoregulation is intact. Explanations for

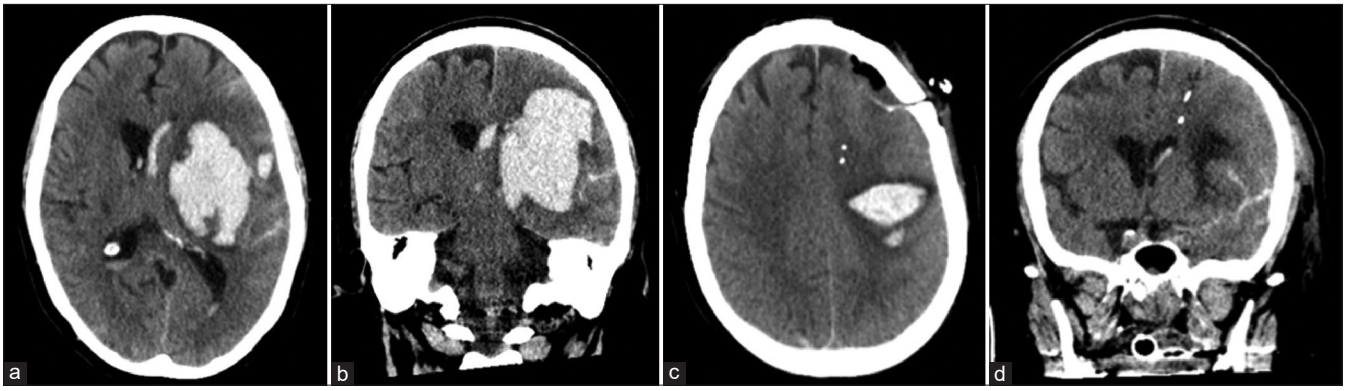

Figure 1: Computed tomography scans. (a) Axial plane view of the brain 10 h before initial surgical evacuation of the intracerebral hemorrhage (ICH). (b) Coronal plane view of the brain 10 h before initial surgical evacuation of the ICH. (c) Axial plane view of the brain 28 h after surgical evacuation of the ICH. (d) Coronal plane view of the brain 28 h after surgical evacuation of the ICH.

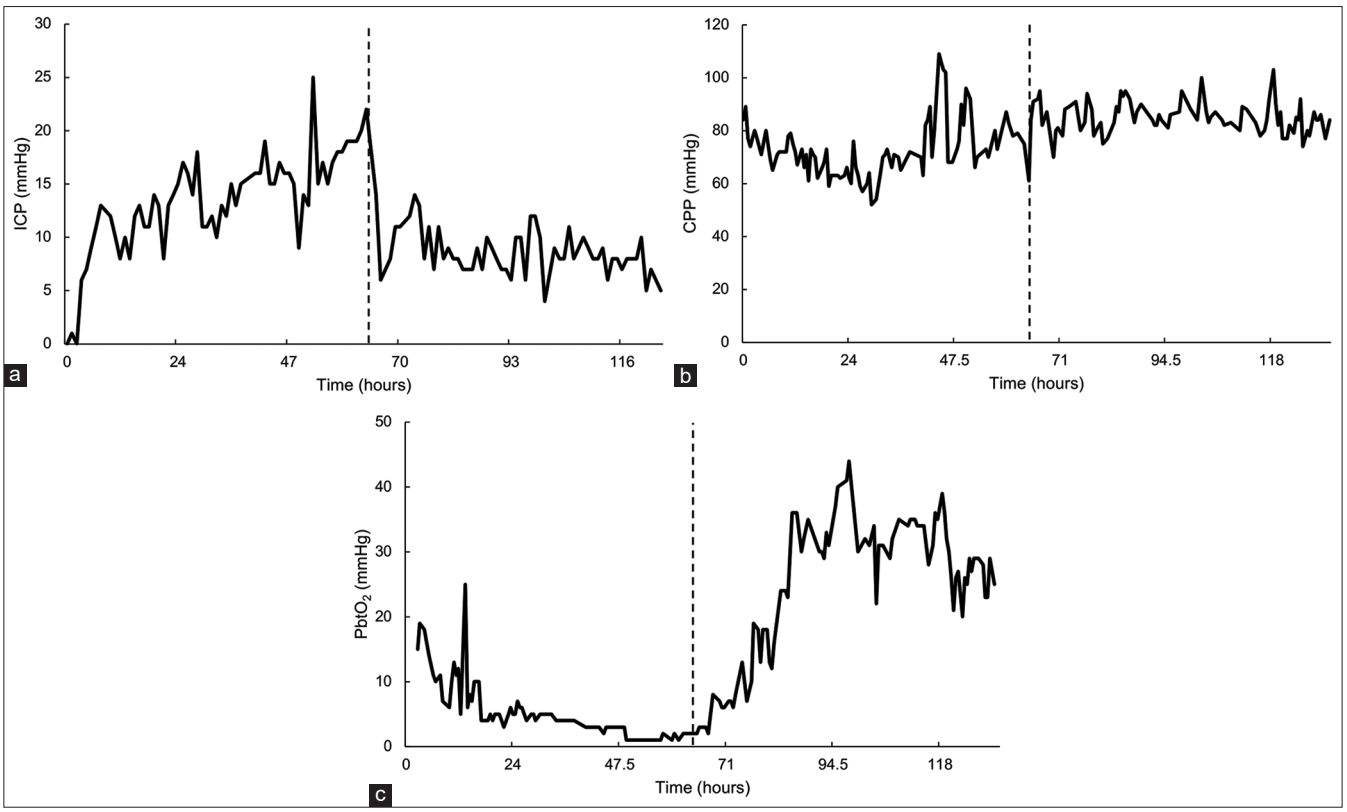

Figure 2: Neuromonitoring data. (a) Intracranial pressure (ICP) versus time. (b) Cerebral perfusion pressure (CPP) versus time. (c) Brain tissue oxygenation ($PbtO_2$) versus time. All neuromonitors were located in the left frontal lobe. Surgery for intracerebral hemorrhage evacuation occurred at 0 h, and surgical placement of the ventriculostomy drain occurred at 62 h (indicated by the dotted black line).

the finding of metabolic crisis despite "normal" ICP include (1) regional lateralized ICP with local CPP compromise in the penumbral zone, (2) peri-hematoma edema increasing local metabolic demand, and (3) disruption of local cerebral autoregulation. This study highlights the utility of metabolic-based multimodal monitoring as a precision medicine device and supports the concept that ICP thresholds may differ between patients.[6]

Placement of EVD after surgical resection in ICH is up to the discretion of the surgical team and is typically dependent on the degree of hydrocephalus. Recent large randomized trials of minimally invasive ICH evacuations suggest surgery is safe and selected patients possibly have mortality and morbidity benefits.[4] With the growing increase in novel surgical treatment of ICH, this study highlights the utility of CMD as a potential triage parameter in post-surgical monitoring.

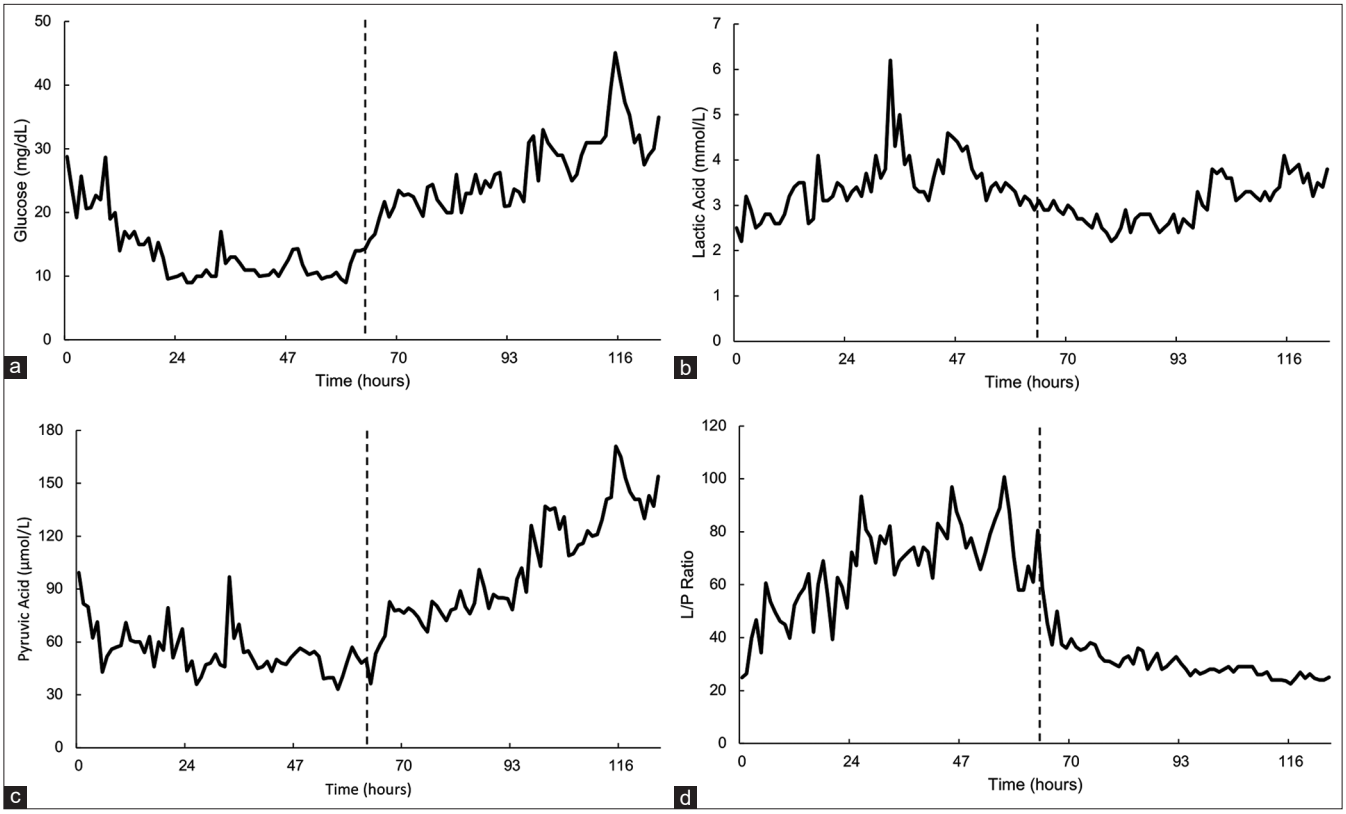

Figure 3: Cerebral microdialysis data. (a) Glucose versus time. (b) Lactic acid versus time. (c) Pyruvic Acid versus time. (d) Lactate to pyruvate (L/P) ratio versus time collected from cerebral microdialysis catheter in the left frontal lobe. All cerebral microdialysis catheters were located in the left frontal lobe. Surgery for intracerebral hemorrhage evacuation occurred at 0 h, and surgical placement of the ventriculostomy drain occurred at 62 h (indicated by the dotted black line).

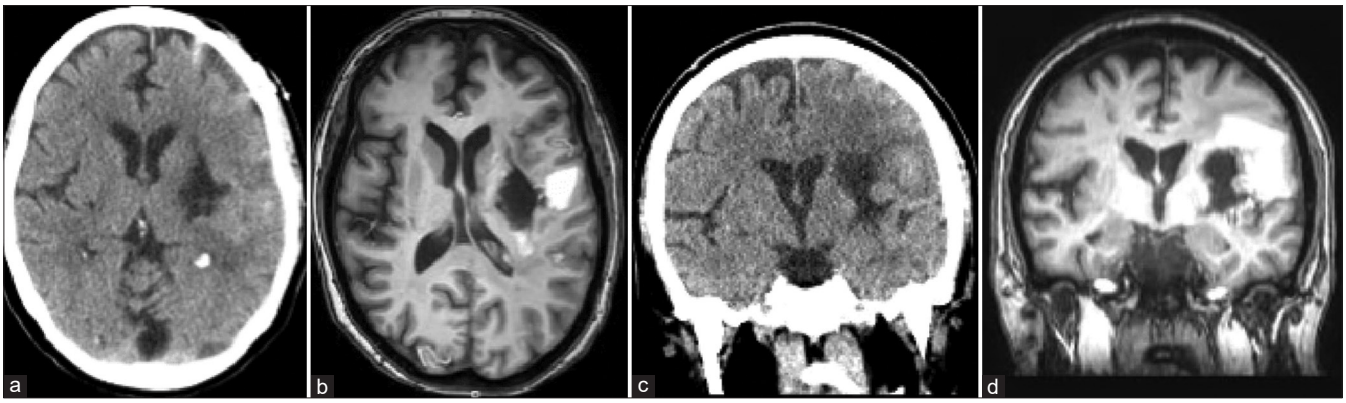

Figure 4: Computed tomography (CT) and magnetic resonance imaging (MRI) images done three weeks after the initial hemorrhage. (a) Axial CT scan through the area of the hemorrhage. (b) Axial T1 MRI scan through the same area. Note the area of increased signal lateral to the area of hemorrhage evacuation that represents residual hemorrhage that was not removed at the time of the BrainPath™ procedure. (c) Coronal CT scan through the area of the hemorrhage. (d) Coronal T1 MRI scan through the same area. Note the area of residual hemorrhage lateral to the area of hemorrhage. There is an overall decrease in mass effect and surrounding cerebral edema on these images taken about three weeks after the initial hemorrhage. The ventriculostomy has been removed. There is no sign of hydrocephalus.

Current knowledge regarding using CMD in sICH is limited; however, CMD has more established clinical benefits in SAH and TBI. In a recent microdialysis study, Rasulo *et al*. observed disturbance of cerebral autoregulation and deranged metabolites in the PHZ for 21 out of 22 patients with sICH.[13] Similarly, in a microdialysis study analyzing the PHZ and normal cortex for sICH, Tobieson *et al*. found alterations in metabolic parameters and higher levels of both

pro- and anti-inflammatory cytokines in the PHZ compared to the normal cortex.[16] With regard to clinical impact, the use of CMD is better established in SAH and TBI, where it allows for early detection of delayed cerebral ischemia and has been correlated to patient outcomes between 3 and 12 months after acute neurological injury.[7,18,19] In patients with delayed cerebral ischemia, CMD has also demonstrated greater specificity than other care modalities, including transcranial Doppler ultrasound and angiography.[18] Our results substantiate these findings and indicate that CMD may have utility in clinical decision-making for patients with sICH after clot evacuation. In this case, CMD catheters in the peri-hematoma zone of edema of a sICH were used to monitor metabolic function surrounding the injury and provided information that helped prevent secondary brain injury.

The results indicate that using an EVD helped attenuate relatively increasing ICPs and allowed for subsequent improvement in brain oxygenation, cerebral blood flow, and metabolism. Although ICP was in the high-normal range after the initial surgery, further lowering of ICP through EVD placement resulted in improved trends in all recorded metabolic parameters. The results suggest that modification of metabolism in the PHZ, monitored by CMD, can improve outcomes by decreasing the area of potential cell death both temporarily and in the long term. These data highlight CMD's utility in understanding the underlying metabolic function and as an adjunct to developing treatment plans in patients with sICH. Further studies should investigate the safety and practicality of CMD in multimodal monitoring and its utility in predicting neurologic outcomes in larger prospective cohorts of ICH.

CONCLUSION

This case illustrates the utility of multimodal brain monitoring to improve the local environment of the brain in response to sICH. We also note the removal of the ICH through a minimally invasive approach, followed by the placement of the EVD, which led to improved brain metabolism in the PHZ despite high-normal ICP. When used in this context, CMD may reveal early signs of metabolic dysfunction, indicating the need for further intervention, which may help improve outcomes in sICH

Declaration of patient consent

Patient's consent not required as patient's identity is not disclosed or compromised.

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Conflicts of interest

There are no conflicts of interest.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

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