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PRACTICAL PEARL

# The CSF Diversion via Lumbar Drainage to Treat Dialysis Disequilibrium Syndrome in the Critically Ill Neurological Patient

Christopher S. Hong[1], Kevin Wang[2] and Guido J. Falcone[3*]



## Introduction

Dialysis disequilibrium syndrome (DDS) is a clinical syndrome of neurologic deterioration resulting from cerebral edema seen in patients undergoing dialysis [1–5]. DDS is most prevalent during or immediately after initial hemodialysis, but may also occur during maintenance hemodialysis, especially in those with preexisting neurological disease [1, 6–8]. Risk factors include initial dialysis, resuming dialysis after missing multiple sessions, markedly elevated blood urea concentration pre-dialysis, severe metabolic acidosis, and preexisting neurologic disease including any condition that increases blood–brain barrier permeability [1, 4, 9–11]. Symptoms are nonspecific, but similar to those of increased intracranial pressure (ICP), including headaches, mental confusion, and coma [1].

The etiology of DDS is unknown, but two prevailing theories of its pathophysiology are the reverse urea effect, in which shifts of urea concentrations create an osmotic gradient promoting cerebral edema [12, 13] and transient intracerebral metabolic acidosis after hemodialysis, which displaces sodium and potassium from organic anions making them osmotically active and resulting in cerebral edema [1, 13]. If left unmanaged, DDS can lead to severe clinical sequelae from highly uncontrolled ICPs, resulting in global anoxic brain injury, seizures, coma, and death.

*Correspondence: guido.falcone@yale.edu
[3] Division of Neurocritical Care and Emergency Neurology, Department of Neurology, Yale School of Medicine, 15 York Street, LCI Room 1004D, Box 208018, New Haven, CT 06520, USA
Full list of author information is available at the end of the article

Traditionally, DDS has been managed with preventative measures aimed at reducing ICP, including manipulation of hemodialysis parameters, use of osmotically active substances, and continuous renal replacement therapy [1, 9, 14]. In this case, we describe the successful treatment of refractory intracranial hypertension during DDS with a lumbar drain and the use of invasive cerebrospinal fluid (CSF) diversion as a novel method of managing ICP crises secondary to DDS in the neurocritical care setting.

## Case Description

A 59-year-old male with type 2 diabetes, hypertension, coronary artery disease, and end-stage renal disease on hemodialysis presented with unprovoked sudden-onset headaches, right-sided weakness, and altered mental status. Computed tomography (CT) of the head demonstrated a left basal ganglia hemorrhage with casting of the right lateral, third, and fourth ventricles with hydrocephalus (Fig. 1a, b). He arrived intubated to our institution's neurological intensive care unit, and an emergent right frontal external ventricular drain (EVD) was placed. Magnetic resonance imaging (MRI) followed by digital subtraction angiography failed to reveal an underlying mass or vascular lesion. He subsequently underwent dialysis uneventfully without ICP spikes and a stable neurological examination while undergoing continued CSF drainage, which was eventually removed on hospital day 12.

Two days after EVD removal, the patient developed altered mental status. Head CT revealed mild progression of ventriculomegaly compared to imaging obtained

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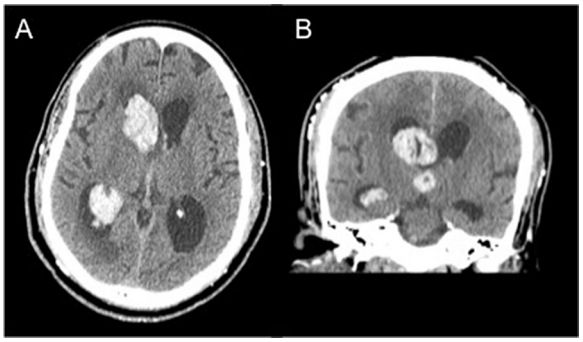


**Fig. 1** Computed head tomography (CT) at time of presentation. Representative **a** axial and **b** coronal images demonstrate right caudate hemorrhage with significant intraventricular extension causing casting of the right ventricular system and radiographic hydrocephalus

at time of EVD removal, but with otherwise absent midline shift and patent cisterns. Electroencephalography did not demonstrate seizure activity. Although CSF cultures from a lumbar puncture did not reveal any evidence to support infection, the patient had been on empiric antibiotics for positive blood cultures growing coagulase-negative staphylococcus. Brain MRI revealed avid ependymal enhancement, which, together with ongoing fevers and a leukocytosis, was consistent with ventriculitis, for which antibiotics were broadened. Six days later, he underwent another planned session of hemodialysis and became acutely apneic and briefly hypotensive requiring re-intubation and up-titration of existing vasopressor administration. Emergent head computed tomography did not demonstrate new hemorrhage or increased cerebral edema and repeat lumbar puncture (opening pressure 18 mm Hg) showed improved cell differential and thus antibiotic response. Cardiac workup was unremarkable with normal continuous telemetry readings and electrocardiograms showing sinus rhythm. At his next dialysis session, he developed recurrent apnea, despite maintaining normotension with ongoing vasopressor support, requiring changes in ventilator settings and demonstrating elevated blood urea nitrogen levels. Likewise, the continuous scalp electroencephalogram demonstrated increased generalized attenuation with occipital–parietal lobe suppression, frequent widespread discontinuity, and marked generalized slowing during dialysis treatment (Fig. 2a, b), suggestive of relative hypotension with decreased cerebral blood flow, particularly in the posterior circulation, and consistent with DDS. A second lumbar puncture was performed at this time to measure ICPs, resulting in a normal opening pressure of 13 mm Hg. However, repeat brain magnetic resonance imaging demonstrated new areas of restricted diffusion

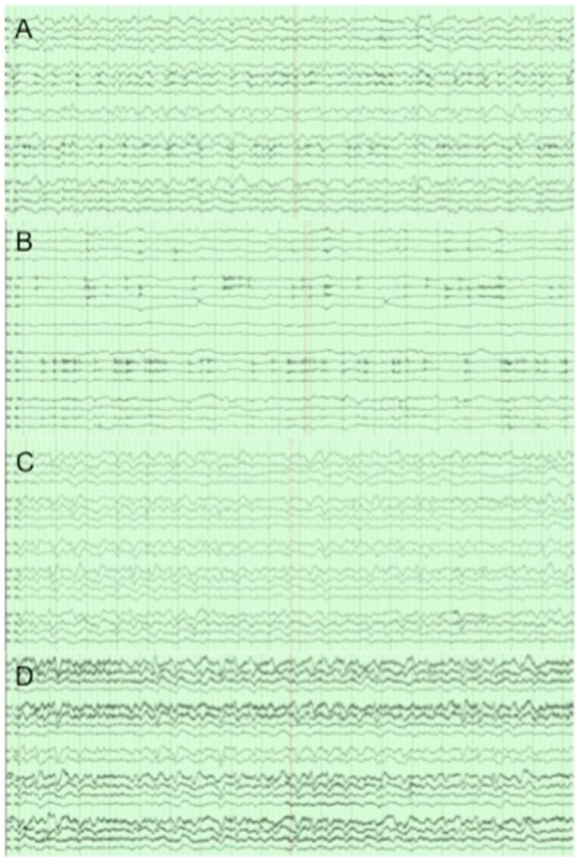


**Fig. 2** Electroencephalography (EEG) recordings. **a** EEG taken prior to lumbar drain placement and dialysis initiation demonstrates predominantly 5–7 Hz theta background with frequent epileptiform discharges, at times become generalized periodic discharges up to 2 Hz. **b** EEG during dialysis, but prior to lumbar drain placement showing abrupt change during dialysis with marked generalized slowing, generalized attenuation with parietal–occipital suppression, and frequent widespread discontinuity consistent with global cerebral hypoperfusion from elevated intracranial pressure. Subsequently, EEG recordings after lumbar drain placement **c** before and **d** after initiation of dialysis show no change in continuous EEG pattern. Both demonstrate a predominately 5–7 Hz theta background with frequent epileptiform discharges as before

in watershed areas, consistent with ischemic lesions secondary to a severe decrease in cerebral perfusion pressure presumably caused by sustained subacutely elevated ICPs. Given the presence of ventriculitis, another EVD was deferred in favor of a lumbar drain, which revealed an elevated opening pressure of 23 mm Hg at time of placement. Subsequently, 30 cc of CSF was removed prior to the patient's next hemodialysis session, which he tolerated on pressure support without any apneic episodes or drops in blood pressure, as measured by a transduced radial arterial line. ICPs after hemodialysis were under 20 mm Hg, measured with the patient supine and the

transducer at the level of the foramen of Monroe. Similarly, the continuous scalp encephalogram did not redemonstrate attenuated areas suggestive of diminished cerebral blood flow (Fig. 2c, d). Two further sessions of hemodialysis were tolerated uneventfully following the same strategy of removing 20 cc of CSF with ICPs under 20 mm Hg after dialysis. Continuous renal replacement therapy was deferred by the nephrology service, given his hemodynamic stability. Over the following days, the patient's examination improved to a point at which he was extubated and could intermittently follow commands. Subsequently, he underwent his fourth hemodialysis session without lumbar drainage, as he was bridged to sodium remodeling to prevent further ICP spikes, and given his clinical stability, the lumbar drain was removed (Table 1). He tolerated the rest of his hemodialysis sessions without further need for CSF diversion and exhibited a stable neurological examination.

**Table 1 Laboratory values surrounding hemodialysis sessions**

| | Na | Glucose | BUN |
|---|---|---|---|
| Session 1 | | | |
| Pre | 141 | 141 | 76 |
| Post | 141 | 120 | 39 |
| Session 2 | | | |
| Pre | 140 | 118 | 63 |
| Post | 140 | 133 | 25 |
| Session 3 | | | |
| Pre | 138 | 197 | 63 |
| Post | 141 | 213 | 33 |
| Session 4 | | | |
| Pre | 143 | 181 | 47 |
| Post | 141 | 122 | 23 |
| Session 5 | | | |
| Pre | 141 | 160 | 47 |
| Post | 144 | 106 | 23 |
| Session 6 | | | |
| Pre | 143 | 161 | 41 |
| Post* | | | |
| Session 7 | | | |
| Pre | 140 | 118 | 32 |
| Post | 141 | 170 | 16 |
| Session 8 | | | |
| Pre | 142 | 159 | 33 |
| Post | 141 | 163 | 17 |
| Session 9 | | | |
| Pre | 141 | 134 | 21 |
| Post | 144 | 131 | 13 |
| Session 10 | | | |
| Pre | 141 | 206 | 20 |
| Post | 142 | 200 | 14 |

Sessions 1–3 were performed with 20–30 cc of CSF drainage from the lumbar drain prior to hemodialysis. Session 4 was performed without CSF drainage, and the lumbar drain was subsequently removed following this session. Sessions 5–10 were performed with sodium remodeling

*Post-dialysis laboratories could not be obtained after session

## Discussion

DDS is a clinical diagnosis, largely of exclusion, among a broad range of differential diagnoses including metabolic causes like uremia, hyponatremia, and hypoglycemia and structural causes from ischemic or hemorrhagic stroke. While no radiological study is diagnostic, diffusion-weighted sequences on brain magnetic resonance imaging may be useful in demonstrating watershed area strokes suggestive of severely decreased cerebral perfusion pressure caused by elevated ICPs [15, 16]. Management of DDS is based primarily on preventative measures aimed at reducing ICP, particularly for patients with high serum blood urea nitrogen at initial dialysis [1]. A short hemodialysis session (2 h) with a low blood flow (200 ml/min) and slow urea removal rate (urea reduction ratio of 0.4) is recommended as the initial prevention for patients at risk of DDS [1, 9, 14]. Continuous renal replacement therapy may also be considered in patients with intracranial mass lesions who are at risk of DDS [7, 14]. Sodium remodeling is an additional effective strategy, in which dialysate sodium is initially maintained at high levels during the start of hemodialysis to support higher osmolality early on and prevent decreases in osmolality from other solute removal. Additionally, the addition of glucose, glycerol, ormannitol, among other osmotically active substances has also been shown to prevent DDS [17–20]. In severe symptomatic cases including seizures, raising plasma osmolality with 23% saline or mannitol and hyperventilation has demonstrated some efficacy [21], but may prove futile necessitating more invasive measures to control ICPs such as CSF diversion [1, 10].

The decision to pursue CSF diversion in our patient was initially based on an empiric diagnosis of DDS, considering opening pressures from lumbar punctures were only mildly elevated at best. Additionally, the systemic hypotension he experienced during his initial HD session that prompted intubation could have caused watershed infarcts. However, the MRI findings of watershed infarcts were likely more attributable to DDS, given that the episode of hypotension was short-lived and rapidly corrected with increased vasopressor support. Furthermore, during the patient's next HD session after intubation, he exhibited recurrent apnea despite maintaining normotension, requiring changes to ventilator settings. Taken together, these observations led us to a presumed diagnosis of DDS, further supported by the fact that after CSF diversion with the lumbar drain, the patient was

successfully weaned off vasopressor support and extubated. As such, in suspected cases of DDS, despite high normal or mildly elevated ICPs, an empiric trial of CSF diversion may be considered.

CSF diversion has been previously utilized for elevated ICP in DDS in a few case studies. One study reported successful ICP normalization via EVD placement in four patients who required hemodialysis following neurosurgical operations with intermittent CSF drainage favored over continuous drainage and concomitant steroids and mannitol administered in most cases [22]. Another study reported the successful reversal of mildly increased opening intracranial (18 mm Hg) and intraocular pressures with the use of an EVD in a child with end-stage renal disease on peritoneal dialysis who developed signs of intracranial hypertension and acute glaucoma while undergoing treatment with recombinant human growth hormone [23]. The patient in this study regained consciousness and experienced a normalization of intraocular pressures. A third study described successful management of elevated ICPs in a pediatric patient with anoxic brain injury and acute kidney failure from cardiac arrest, in which ICPs were reduced to 3 mm Hg with CSF diversion from an EVD prior to dialysis until she could be weaned off CSF drainage with eventual renal recovery [24].

Although previous case series have documented increases in ICP via invasive monitoring during hemodialysis, particularly in patients with traumatic brain injury [7, 25], there is sparse evidence regarding ICP thresholds that may be necessary to undergo dialysis successfully without neurological sequelae in patients with DDS. Lund et al. described successful management of elevated ICPs in a pediatric patient with anoxic brain injury and acute kidney failure from cardiac arrest, in which ICPs were reduced to 3 mm Hg with CSF diversion from an EVD prior to dialysis until she could be weaned off CSF drainage with eventual renal recovery [24]. In our patient, we utilized empiric CSF drainage of up to 30 cc immediately preceding dialysis to anticipate rises in ICP during hemodialysis sessions. This strategy successfully managed the patient through a further three sessions of hemodialysis without cardiopulmonary events, subsequently allowing for cessation of CSF drainage and transition to sodium remodeling. In patients for whom EVD placement is suboptimal (i.e., infection, small ventricles, existing intracranial injury), alternative CSF drainage of 20–30 cc immediately via a lumbar drain may be an effective strategy to mitigate the anticipated rises of ICP during hemodialysis in patients with DDS. Further reports correlating ICP responses to the volume of CSF drained in the peritoneal dialysis period are needed to delineate optimal CSF diversion in patients with DDS.

As our case suggests, lumbar drainage may be a viable and preferable alternative of distant and sterile catheter placement in patients with ventriculitis, secondary to prolonged EVD placement. However, caution must be taken not to utilize lumbar drainage in patients with obstructive CSF outflow dynamics to avoid risk of downward herniation. A potential disadvantage of CSF diversion with lumbar drainage may be reduced ease in monitoring ICPs in patients, compared to an EVD. However, ICPs may still be measured via lumbar drain by setting the zeroing the system, while the patient is fully flat and measuring pressure recordings, likewise, in this same position to negate the effects of gravity. As our case indicates, alternative modalities to monitor ICPs may also be used, such as scalp encephalogram monitoring for cerebral blood flow as a surrogate for ICPs and, importantly, the clinical examination in those patients with sufficiently recovered neurological function.

## Conclusions

There remains no established effective treatment for DDS once neurological symptoms have set in. The medical landscape surrounding DDS centers on preventative measures that involve adjusting the rate, timing, and solute concentrations used in hemodialysis, but very little has been explored in the way of preventive and therapeutic strategies for DDS besides supportive care or stopping hemodialysis. This case describes CSF diversion via less invasive lumbar drainage over EVD placement as a management option in DDS, particularly in patients with existing contraindications to EVD placement such as ventriculitis. As such, CSF diversion via a lumbar drain may be an effective alternative and/or adjunct to medical therapies for the monitoring and treatment of refractory elevated ICPs during dialysis in patients with existing intracranial injuries.

**Author details**

[1] Department of Neurosurgery, Yale School of Medicine, New Haven, CT 06520, USA. [2] Department of Neurology, Yale School of Medicine, New Haven, CT 06520, USA. [3] Division of Neurocritical Care and Emergency Neurology, Department of Neurology, Yale School of Medicine, 15 York Street, LCI Room 1004D, Box 208018, New Haven, CT 06520, USA.

**Authors' contributions**

CSH and KW collected data and drafted the manuscript. GJF supervised this work and provided critical revisions to the manuscript.

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**Conflict of interest**

The authors declare that they have no conflict of interest.

**Ethical Approval/Informed Consent**
The information presented in this report belongs to a patient enrolled in the Yale Acute Brain Injury Registry and Tissue Repository, a longitudinal study of patients admitted to the Yale Neurosciences Intensive Care Unit approved by the local IRB.

## Publisher's Note



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