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Severe hyperglycorrhachia and status epilepticus after endoscopic aqueductoplasty: illustrative case

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BACKGROUND While hypoglycorrhachia is observed and managed frequently, there are few reports in the literature of clinically significant hyperglycorrhachia after neurosurgery. Understanding the effects and management of severe hyperglycorrhachia is important to the neurosurgeon and neurocritical care teams who care for patients in these rare scenarios.

OBSERVATIONS The authors present the case of a 3-month-old male with congenital hydrocephalus who faced profound hyperglycorrhachia and status epilepticus after an endoscopic aqueductoplasty using an irrigant composed of lactated Ringer's solution with dextrose 5% in water. A multidisciplinary approach was developed to monitor and treat the patient's seizures and cerebrospinal fluid (CSF) osmolytes.

LESSONS This case provides several learning opportunities for understanding CSF physiology, pathogenesis of common brain injuries related to osmotic shifts and inflammatory states, as well as clinical management of hyperglycorrhachia. It also reiterates the significance of meticulous intraoperative assessment to avoid preventable medical errors.

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KEYWORDS hyperglycorrhachia; neurocritical care; endoscopy; seizure

Under physiological conditions, the blood–brain barrier maintains ionic homeostasis within the cerebrospinal fluid (CSF). In several diverse pathological conditions, which include infectious meningitis, stroke, and malignancy, perturbations in this homeostasis may cause hypoglycorrhachia. In contrast, hyperglycorrhachia is rarely reported in the literature, but when described, it has been attributed to iatrogenic causes from systemic hyperglycemia.[1,3] Hyperglycorrhachia has been shown to induce neuronal hyperexcitability with seizures and myoclonus. The effects of hyperglycorrhachia on CSF dynamics and clearance for management in the acute setting have not been previously described. Similarly, the long-term impact on future neurological development and epilepsy is not known.

Illustrative Case

A male infant was born at 38 weeks' gestation with congenital hydrocephalus due to intraventricular hemorrhage identified in utero. Head magnetic resonance imaging (MRI) demonstrated triventricular hydrocephalus with stenosis of the cerebral aqueduct (Fig. 1). His physical exam was notable for an enlarging head circumference, but his neurological exam was otherwise benign. Surgical options, which included endoscopic third ventriculostomy (ETV), ventriculoperitoneal shunt placement, and endoscopic fenestration with aqueductoplasty, were offered nonurgently when the patient reached 3 months of age. Considering the potential for future revisions with shunting and the 50% predicted failure rate calculated by the ETV success score, the family elected to proceed with endoscopic aqueductoplasty. At the time of surgery, intraventricular access was obtained via a right frontal approach using standard neurosurgical endoscopic techniques. However, mistakenly, irrigant for the endoscope was lactated Ringer's solution with additive dextrose 5% in water (D5W) instead of the usual nonadditive formulary. The irrigant was exchanged with the correct solution early in the case, but the effect of the already administered irrigant was of unknown consequence. The remainder of the case proceeded uneventfully with

ABBREVIATIONS CSF = cerebrospinal fluid; D5W = dextrose 5% in water; EEG = electroencephalography; ETV = endoscopic third ventriculostomy; IV = intravenous; MRI = magnetic resonance imaging.

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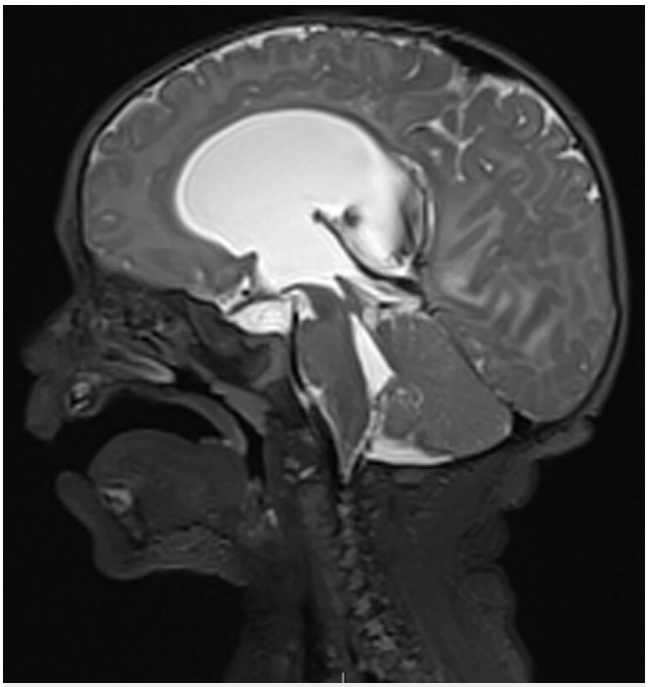

FIG. 1. Preoperative sagittal T2-weighted magnetic resonance (MR) image demonstrating ventriculomegaly with aqueductal stenosis.

endoscopic fenestration of the aqueduct and placement of an aqueductal stent connected to a subgaleal reservoir. This was completed with technical success and without identifiable neuronal injury.

Postoperatively, the patient was extubated and transferred to the recovery unit without deficit. Shortly thereafter, during routine postoperative imaging (Fig. 2), the patient developed hypercarbic respiratory failure with altered mental status associated with left head-turning and left arm-jerking movements. He was reintubated emergently with propofol sedative and given lorazepam and levetiracetam loading doses before he was transferred to the pediatric intensive care unit for escalation of care. Repeat head computed tomography demonstrated stability with no evidence of hemorrhage or other acute changes. He continued to have leftward gaze deviation as well as left head turning. Intranasal midazolam was given for concerns of nonconvulsive status epilepticus, with normalization of eye deviations after administration. Seizure activity was monitored with continuous electroencephalography (EEG), which demonstrated multiple electrographic seizures without a clinical correlate arising from the right frontotemporal region. Serum glucose and serum sodium were within normal limits. CSF was aspirated via reservoir tap, and CSF glucose measured 1464 mg/dL.

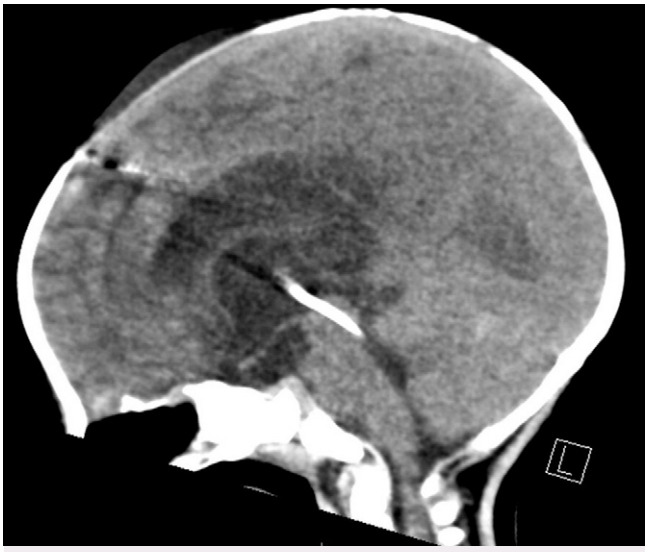

FIG. 2. Postoperative sagittal computed tomography (CT) scan demonstrating interval placement of an aqueductal stent with a slight decrease in ventricular size and pneumocephalus but without acute hemorrhage.

A multidisciplinary approach among the intensive care unit, neurology, and neurosurgery teams was developed to manage the hyperglycorrhachia. Intravenous (IV) normal saline was administered at a rate 2 times the calculated maintenance dose. Frequent blood draws were ordered to trend electrolytes. To preserve euvolemia, diuretic furosemide was given every 12 hours and as needed. The following morning, CSF was rechecked and CSF glucose had decreased to 154 mg/dL, with serum sodium and glucose values that remained within normal limits. Neurological exam returned to baseline, and EEG electrodes were removed. The patient was transferred to the floor and discharged on postoperative day 3 in stable condition.

After discharge, the patient returned to the hospital at 2 weeks with increasing subgaleal fluid around his hardware and an increase in ventricular size on head ultrasound. His subgaleal reservoir was converted to a ventriculoperitoneal shunt during this inpatient stay. Within the first year after the index surgery, he required a total of 2 additional shunt revisions due to valve obstruction and proximal catheter obstruction on separate admissions. At the 5-year follow-up, the patient had continued to meet age-appropriate milestones and remained developmentally on target. However, he has had recurrent seizures and now has an established diagnosis of focal epilepsy. His seizure semiology includes behavioral arrest, blank staring, and upward eye deviation to the left lasting less than 1 minute. He remains on levetiracetam and lacosamide maintenance antiepileptics.

Patient Informed Consent

The necessary patient informed consent was obtained in this study.

Discussion

Observations

We present the case of a 3-month-old boy with congenital hydrocephalus who faced profound hyperglycorrhachia and status epilepticus after an endoscopic aqueductoplasty using an irrigant composed of lactated Ringer's solution with D5W. This case represents the first report in the literature of a clinically significant hyperglycorrhachia after neurosurgery and only 1 of 3 case studies identifying iatrogenic hyperglycorrhachia as a cause of seizure.[1,3]

At a molecular level, the patient's pathophysiology can be explained by significant perturbations in both CSF–brain ionic homeostasis and CSF dynamics, which resulted in damaging effects on neurons both physically and neurochemically. The CSF–brain interface is reinforced with gap junctions that demonstrate permeability to macromolecules between the ventricular compartment and brain

interstitial fluid.[2] As such, the distribution of various molecules across the barrier endows the CSF compartment with the essential function of maintaining a balanced chemical neuronal milieu.[2]

Under normal physiological conditions, glucose enters the CSF from the plasma via facilitated diffusion in a bidirectional fashion, influenced by the concentration of plasma glucose levels. Multiple studies of the relationship between CSF and serum glucose levels have shown that, in the pediatric population, the CSF glucose level is normally approximately 60% of the serum glucose level during childhood, in the range of 50–80 mg/dL.[4] Furthermore, the normal production rate of CSF is 0.35 mL/minute or approximately 450 mL/day, with a total CSF volume of 65–140 mL in children and 90–150 mL in adults.[2] This is equivalent to a CSF turnover rate approximating 5–7 hours.[5,6]

We propose that the induced iatrogenic hyperglycorrhachia resulted in a significant alteration of the neuronal ionic homeostasis, resulting in the osmotic shift of brain parenchymal extracellular fluid into the CSF compartment. Acute osmotic shifts are well-recognized causes of brain injury in osmotic demyelination syndromes, salt intoxication, and dialysis disequilibrium. With the acuity of the chemical perturbation in the neuronal extracellular compartment, neurons were not able to regain homeostasis by adjusting and increasing the production of intracellular osmoles. This neurochemical instability may then have led to disorganized neuronal transmission and hyperexcitability, manifesting in a clinical seizure. Based on the degree of hyperglycorrhachia, the calculated osmotic shift was equivalent to a change in serum sodium of 44 mmol/L, which would be expected to result in death or devastating injury. Fortunately, in this case, injury was limited, and reversal was promptly achieved in a calculated fashion. Interestingly, a high systemic glucose concentration, aside from its osmotic effects, has also been postulated to induce cytokine release in patients with traumatic brain injury, which further exacerbates their recoveries. We believe that it is possible that there may have been a similar proinflammatory effect induced by the abundance of glucose in the CSF in our patient.[7]

With regard to CSF dynamics in this case, the clearance function of CSF may have been impaired by CSF stasis attributed to its hyperosmolar concentration. This, in turn, would have resulted in inefficient excretion of neuronal catabolites manifesting in both seizures and cognitive impairment. Based on the aforementioned normal CSF dynamics values, a calculated rate of IV isotonic fluid infusion and diuretic was used to reduce the CSF glucose concentration and reestablish the physiological CSF fluid regulation mechanism.

Hyperglycorrhachia is typically observed only alongside evidence of concurrent systemic hyperglycemia. Glucose in the CSF normally ranges between 50 and 80 mmol/L, or approximately two-thirds the plasma concentration of glucose. While the differential for hypoglycorrhachia includes neoplastic processes, infection, or systemic hypoglycemia, the differential for hyperglycorrhachia appears limited to systemic hyperglycemia and iatrogenic causes. The 2 other reports in the literature by Katz et al.[2] and Bass and Lewis[1] share patients with hyperglycorrhachia due to extravasation of parenteral nutrition into the CSF space and direct communication from a misplaced central venous catheter into a paravertebral vein, respectively. In accordance with our findings, these studies illustrated that the high glucose content in the CSF caused neurological hyperactivity with medically refractory seizures and segmental myoclonus, respectively. CSF was initially accessed at varying time points in these reports. Therefore, in hospitalized patients undergoing procedures presenting with acute-onset, first-time seizures, clinicians should exercise a high degree of suspicion. CSF studies obtained in a timely manner will assist in diagnosis and monitoring.

Once diagnosed, a multidisciplinary approach helps to stabilize the patient and terminate seizure activity. As in this case, we recommend admitting these patients to an intensive care unit for airway management, resuscitation, close seizure monitoring, and the administration of antiepileptic medications. After stabilization, seizures are likely to stop with the correction of CSF glucose, making hyperglycorrhachia the priority. It is imperative to refrain from administering insulin as would be done in cases of high serum glucose; doing so induces systemic hypoglycemia in patients with otherwise normal serum glucose concentrations. The glucose in CSF must re-enter into the blood before excretion. The administration of isotonic maintenance fluids promotes CSF production and also provides a favorable osmotic gradient, which together promote recirculation of CSF glucose into the plasma. Aggressive correction, however, may cause rapid osmotic shifts, which can precipitate cerebral edema. Careful fluid balance, electrolyte monitoring, and serial neurological exam are imperative to prevent further neurological injury.

The correlation between the patient's index surgery and his evolving course is uncertain. We postulate that the hyperglycorrhachia may have had an inflammatory effect in the CSF despite resolution of the CSF glucose. At the first revision, 1 month from the initial shunt placement, proteinaceous debris was noted to have obstructed the shunt valve and required replacement. During the second revision, 3 months from the initial shunt placement, the proximal catheter had malfunctioned. The catheter was gently removed but was adherent and had membranous tissue around it. We speculate that neuroinflammation from the inciting event affected the CSF viscosity and may have played a role in the development of these subsequent failures. Last, there is not sufficient evidence to support hyperglycorrhachia as a cause of focal epilepsy, but this case does raise the possibility that the patient's index surgery resulted in nonradiographic neuronal injury. Fortunately, the patient has since progressed appropriately from a developmental standpoint.

Lessons

We present the case of a 3-month-old boy with congenital hydrocephalus who faced profound hyperglycorrhachia and status epilepticus after an endoscopic aqueductoplasty using an irrigant composed of lactated Ringer's solution with D5W. While hypoglycorrhachia is clinically observed and managed frequently, to the best of our knowledge, this case represents the first report in the literature of clinically significant hyperglycorrhachia after neurosurgery and only 1 of 3 case studies identifying iatrogenic hyperglycorrhachia as a cause of seizure. Although this case represents a rare clinical scenario, the case provides several learning opportunities for understanding CSF physiology, the pathogenesis of common brain injuries related to osmotic shifts and inflammatory states, as well as the clinical management of hyperglycorrhachia. It also reiterates the significance of meticulous intraoperative assessment to avoid preventable medical errors.

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Disclosures

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author Contributions

Conception and design: Kaufman. Acquisition of data: Masri, Kaufman. Analysis and interpretation of data: Dharia, Masri, Kaufman. Drafting of the article: Dharia, Masri, Rilinger, Kaufman. Critically revising the article: Dharia, Rilinger, Kaufman. Reviewed submitted version of the manuscript: Dharia, Rilinger, Kaufman. Approved the final version of the manuscript on behalf of all authors: Dharia. Study supervision: Kaufman.

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